THE EFFECT OF MOLECULAR GEOMETRY ON THE ELECTRONIC EFFECTS OF THE AZO AND AZOXY GROUPS

A thesis
submitted in partial fulfilment of
the requirements for the Degree
of
Doctor of Philosophy in Chemistry
in the
University of Canterbury
Christchurch, New Zealand
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1986

TABLE OF CONTENTS

LIST OF TABLES

ABSTRACT

The effect of molecular geometry on the electronic effect of the azo and azoxy groups has been examined in two ways.

In Part I the pKa's of a series of substituted benzoic and phenylacetic acids were measured in 50% 0.1MKCl-ethanol at 25°. The results were interpreted in terms of the Hammett equation to derive σ_m, σ_p and σ_p° substituent constants. In addition the rates of solvolysis of a series of aryldimethylcarbinyl chlorides were measured in 87.5%, 80% and 72.5% acetone-water at 25°, with the results being interpreted in terms of σ_p^+ substituent constants. The electronic effect of the following groups was investigated in this way; phenylazo, (σ_m, σ_p, σ_p°, σ_p^+); arylazo, (σ_p^+); 2,6-dimethylphenylazo, (σ_p^+); t-butylazo, (σ_m, σ_p, σ_p^+); phenyl-ONN-azoxy, (σ_m, σ_p, σ_p^+); and phenyl-NNO-azoxy, (σ_m, σ_p). The results suggested that the phenylazo group was in a coplanar configuration with respect to the ring bearing the reaction site. The electronic effect of these substituents in the non-planar configuration was also investigated by determining the effect on σ_p and σ_p^+ when the coplanar configuration was hindered by two flanking methyl groups. The results showed that the non-planar configuration is intrinsicially more electron donating than the coplanar one. The relevance of these results to the different reported assessments of the activating power of the phenylazo group in electrophilic aromatic substitution is discussed.

In Part II the ^{13}C n.m.r. spectra of a series of 3'- and 4'- substituted 2,6-dimethylazobenzenes have been measured in deuterochloroform. The effect of substituents in one ring on the chemical shift of the carbons in the other were interpreted in terms of their inductive and resonance effects by means of a dual substituent parameter analysis. The results showed that relative to the previously reported unhindered azobenzene series, a significant increase in the sensitivity to both inductive and resonance effects was observed at all positions. Possible explanations for this effect in terms of the modes of operation of the inductive and resonance effects are discussed.

INTRODUCTION

1. The Electronic Effect of Substituents

The chemist's understanding of the electronic effects of substituents was quite well developed by the mid 1930's. It was recognised that certain substituents, termed electron withdrawing substituents, encouraged the development of negative charges and discouraged the development of positive charges, while other substituents, termed electron donating, had the opposite effect. Several other important observations had also been made. Substituents that were electron donating (or withdrawing) in one reaction were found to be electron donating (or withdrawing) in most other reactions as well. Furthermore, for a series of substituents the relative order of their substituent effects were normally found to be independent of the reaction. This was found to be especially so in the reactions of *meta* and *para* substituted benzene derivatives, situations where steric effects were unlikely to be important.

In attempting to correlate these experimental observations on a quantitative basis, L.P. Hammett[1] constructed a number of log-log plots of reaction rates or equilibrium constants in the reactions of *meta* and *para* substituted benzene derivatives. In these the logarithm of the reaction rate or equilibrium constant for a derivative containing a particular substituent in one reaction is plotted against the logarithm of the reaction rate or equilibrium constant for the same substituent in another reaction. Hammett noted that for a series of substituents such plots often gave straight lines.

In 1940 he chose a single standard reaction to which he would compare all other reactions to.[2] This led to the formulation of the equation that now bears his name:

$$\log {}^{k^X}/_{k}H \text{ (or } \log {}^{K^X}/_{K}H) = \rho\sigma_{(x)}$$

The symbol σ, he called the substituent constant and defined as the relative electronic effect of a substituent in the standard reaction. Hammett chose the ionization of benzoic acids in water at 25° as the standard reaction and so the substituent constant is defined as the difference in the logarithms of the ionization constants of benzoic acid and the substituted benzoic acid. For example, for a *meta*-chloro substituent, $\sigma_{m\text{-}Cl}$ = log Ka (benzoic acid) - log Ka (*meta*-chlorobenzoic acid). The σ value for the unsubstituted derivative, (X=H) is therefore zero, electron withdrawing substituents have positive σ values, while electron donating substituents have negative σ values.

The symbol ρ he called the reaction constant since it depended on the reaction being studied and was independent of the substituent. The ρ value measures the sensitivity of the reaction to substituent effects. For a given reaction, a positive ρ value indicates that the reaction rate increases as the electron withdrawing power of the substituents increases, while a negative ρ value indicates that the reaction rate decreases as the electron withdrawing power of the substituent increases.

The electronic effect of a substituent is considered to be nett effect of two different ones, the inductive and resonance effects. The inductive or polar effect is

believed to originate from the dipolar character of the substituent. The mechanism by which this dipolar effect is transmitted from the substituent to the reaction site has been the subject of much debate, with several mechanisms being proposed. At the present[3] the concensus of opinion is that the greatest influence on the reaction site due to the inductive effect is the electric field generated by the substituent dipole. The term "inductive effect" is therefore a misnomer since it is, in fact, a field effect, but still remains in common use.

Inductive effects are given the symbol I, with electron withdrawing substituents given a negative sign (-I), and electron donating ones a positive one (+I). The magnitude of a substituent's inductive effect is assumed not to change during the course of a reaction and to be independent of the rest of the molecule.

The resonance (or mesomeric) effect arises as a result of the overlap between the π orbitals of the substituent and the π orbitals of the rest of the molecule. This overlap results in a change in the distribution of the π electrons. Overlap between the π orbitals of the substituent and the reaction site can occur and when this happens, the stability of the reaction site can potentially be changed to a greater extent than that due to inductive effects. Since the reaction site itself is involved with resonance interactions, the resonance effect should vary from reaction to reaction. However in many cases it remains relatively constant.

Resonance effects are given the symbol R, and in line with inductive effects, a +R substituent is a π electron

donor by resonance, and a -R substituent a π electron withdrawer.

For convenience the inductive and resonance effects are assumed to be independent, (although this is unlikely to be strictly correct) and the Hammett σ constant may be expressed in the form:

$$\sigma^X = \sigma_I^X + \sigma_R^X$$

The inductive term σ_I^X for substituent X is reaction independent and constant, whereas the resonance term, σ_R^X is variable and depends on the reaction. In some situations σ_R^X can be reaction independent. This is when either the substituent X is *meta* to the reaction site, or when it is *para* to the reaction site but no direct resonance interaction between it and the reaction site is possible. (This does not imply that $\sigma_R^X(meta) = \sigma_R^X(para)$.) Such a lack of resonance interaction between *para* substituents and the reaction site can occur, for example, when the reaction site is insulated from the π system of the molecule by a saturated linkage, (e.g. a methylene group, $-CH_2-$), or in situations where the substituent and reaction site are both +R groups, or both -R groups.

The σ constants compiled by Hammett from benzoic acid ionizations are assumed to have negligible resonance interaction between the substituent and the reaction site, (this is in fact a slight over-simplification and will be discussed later). When the substituent and the reaction site do interact, the original Hammett equation has to be modified to allow for these interactions. There have been a considerable number of attempts at dealing with this problem, but we will consider only two of these, the

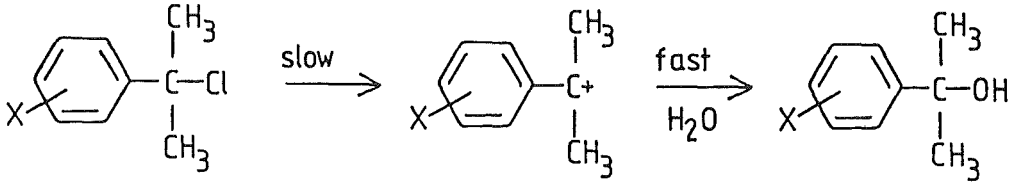
development of different fixed σ scales, and the Dual Substituen Parameter equation.

Hammett had noted that in reactions where a strong -R substituent was *para* to a strong +R reaction site, the normal σ_p constant derived from the benzoic acid ionizations, did not fully take into account the reactivity observed.[4] A similar situation was observed in reactions where strong +R substituents were *para* to strong -R reaction sites. The approach adopted by Hammett for +R reaction sites, and subsequently extended to -R reaction sites by Brown and Okamoto,[5] was to assign the substituents another σ value for use in these situations. Therefore, for *para* substituents capable of exerting a resonance effect, two σ constants are required, one for "normal" reactions, and another "exalted σ constant" of greater magnitude for reactions where substantial interaction with the reaction site exists. This approach appears to work well since situations requiring "intermediate" σ values seem to be rather uncommon.

The "exalted" -R σ values (referred to by Hammett as "nucleophilic" substituent constants) were found to be needed mainly in the reactions of phenols and amines. Their magnitudes were evaluated statistically from a selection of such reactions. Originally they were given the symbol σ*, but they are now universally called σ^- values.

Reactions that require "exalted" σ values for +R substituents (called σ_p^+ values) are much less common, but an important reaction where these σ_p^+ values do apply is electrophilic aromatic substitution. Brown and Okamoto determined the σ_p^+ values for most of the common +R groups

in 1958 by measurement of the rates of solvolysis of a series of aryldimethylcarbinyl chlorides in 90% aqueous-acetone. This reaction proceeds by an S_N1 mechanism and has a highly electron-deficient transition state:



The σ_p^+ values, (or electrophilic substituent constants), obtained from this reaction correlated well with other aromatic reactions where a similar electron deficient reaction site is present.

The assumption that benzoic acid-based σ values involved negligible resonance interaction between the substituent and the side chain was shown to be incorrect by Taft[6] and Wepster[7] independently. They established that the basic σ_p values for +R substituents did contain a slight resonance component arising from the interaction of the substituent and the carboxy group. Both showed that for +R substituents the benzoic acid based σ values were slightly more negative than they would have been had such interactions not been present. The differences however were relatively small for all but the stronger +R groups. Each proposed a new scale of σ values where such interactions were absent. Wepster gave his values the symbol σ^n and Taft σ^o.

The second approach to the problem of variable resonance effects that we will examine is that proposed by Ehrenson, Brownlee and Taft,[8] where the total electronic effect of a substituent is resolved into inductive and resonance contributions, each with its own ρ and σ value. They rewrote the Hammett equation in a more general form:

$$\log {}^{k^{XY}}/_{k^{H}} \text{ (or } \log {}^{K^{XY}}/_{K^{H}}) = \rho_I\sigma_I + \rho_R\sigma_R$$

This equation is known as the Dual Substituent Parameter (DSP) equation.

The authors had hoped that a single σ_R scale could be used in all reactions where previously the $\sigma^-/\sigma/\sigma^+$ scales had to be used. But this proved not to be the case, and in practice different σ_R's were needed for different reactions. A compromise was reached where the σ_R values were chosen from a number of σ_R scales, with the scale that statistically gave the best correlation with the data being used. The choice of σ_R scales for -R substituents was between σ_R° and σ_R^-, and for +R substituents, the σ_R°, σ_R^{BA} and σ_R^+ scales. These σ_R scales were developed statistically by Ehrenson and co-workers and correspond approximately to (i) the resonance components of σ in a system where direct resonance interaction between the substituent and the reaction site was not possible (σ_R°), (ii) that present in benzoic acid reactions (σ_R^{BA}), (iii) that in Hammett's σ^- scale (σ_R^-) and (iv) to that in Okamoto and Brown's σ^+ scale (σ_R^+).

The σ_I scale used with these was based on results obtained in systems where the resonance effects were found to be unimportant.

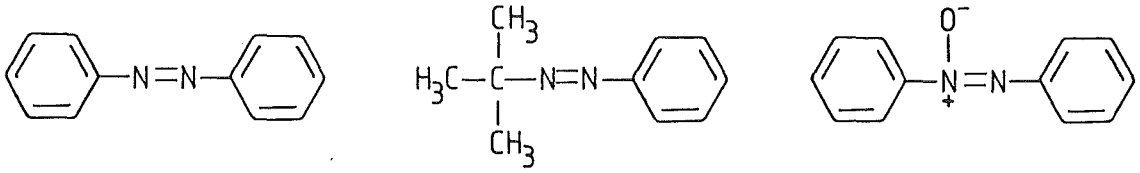
The DSP equation differs from the earlier two-value approach in practice because it relaxes the requirement that $\rho_I = \rho_R$. This may lead to erroneous conclusions with reactivity data where, because the equation cannot vary the σ_R scales to give an intermediate σ_R value, it must instead alter the ρ_I and ρ_R values. However it is useful for the interpretation of spectroscopic data, where ρ_I and ρ_R are

occasionally very different (for example, ^{13}C n.m.r. chemical shifts of *para* ring carbons in monosubstituted benzenes).

In Part I of this thesis the investigation of the electronic effects of substituents has been carried out by the evaluation of σ values. We have restricted ourselves to the "classical" approach by measuring and discussing σ_m, σ_p°, σ_p, σ^- and σ_p^+ constants for our substituents. In Part II however, when the influence of the electronic effects of substituents on the ^{13}C n.m.r. chemical shifts of azo compounds is examined, it proved necessary to interpret the results in terms of the DSP equation.

2. A Note on the Nomenclature of Azo and Azoxybenzenes

The key compounds investigated in this thesis are all derivatives of azobenzene (I), t-butylazobenzene (II) or azoxybenzene (III).



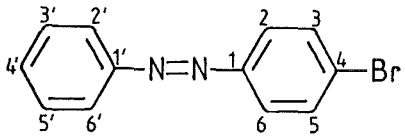
(I) (II) (III)

Several methods have been used for naming these systems, with each method offering its own advantages, but none being suited to all situations. It was decided that in this thesis it was desirable to adhere to one throughout as far as possible.

The "Chemical Abstract Method" as described by IUPAC[9] for azo and azoxybenzenes was the one adopted. It may be summarised as follows:

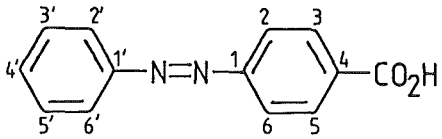
In naming substituted azobenzenes and azoxybenzenes, the method allows the use of either the substituent as the prefix, or the phenylazo (or phenylazoxy) group as the prefix.

The bromo and cyano derivatives have been named as substituted azobenzenes or azoxybenzenes, e.g.



4-Bromoazobenzene

All other compounds have been named as benzene derivatives, with the phenylazo, t-butylazo* and phenylazoxy groups being used as prefixes, e.g.



4-Phenylazobenzoic Acid

In describing azoxybenzene isomers, three cases exist. (i) When the oxygen position is unknown or immaterial, the azoxy name is retained with no prefixes added, for example, for an isomeric mixture 4-bromo substituted azoxybenzenes, the name 4-bromoazoxybenzene is used.

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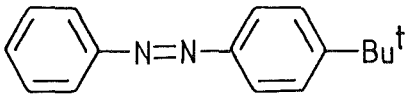
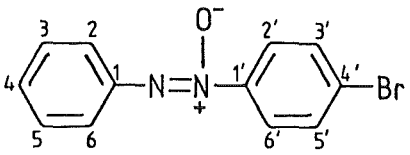
* The t-butylazo group has been used where possible as a prefix to avoid possible confusion between (II) and t-butyl substituted azobenzene, for example (IV). The major exception is in the Appendix.

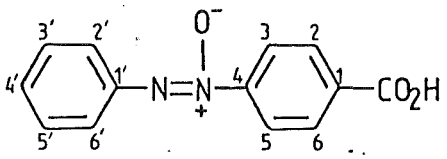


(IV)

(ii) When the oxygen position is known and it is on the nitrogen closer to the ring bearing the substituent(s), then the infix NNO is inserted, e.g.

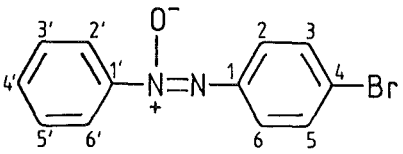


4'-Bromo-NNO-azoxybenzene

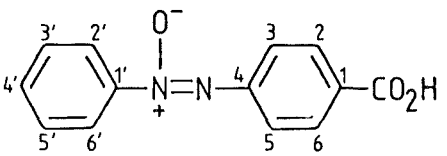


4-Phenyl-NNO-azoxybenzoic Acid

(iii) When the oxygen atom is on the nitrogen that is the more distant from the ring bearing the substituent(s), then the infix ONN is used instead, e.g.

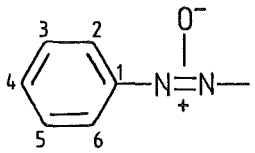


4-Bromo-ONN-azoxybenzene

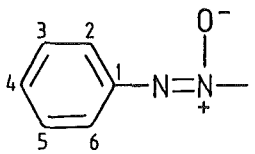


4-Phenyl-ONN-azoxybenzoic Acid

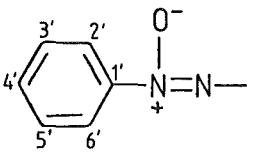
An exactly analogous approach is adopted naming azoxy groups using the prefix system, e.g.



Phenylazoxy (unspecified)



Phenyl-NNO-azoxy



Phenyl-ONN-azoxy

The numbering of the ring carbons depends on whether the phenylazo or the substituent name is used as the prefix. It is important to note the difference between the two as confusion can arise. This problem is most acute in the listing of carbon-13 n.m.r. data. For these, in the experimental section both methods have been used, depending on the substituent criteria set out above. However in the tables of data in the Appendix, all the compounds are named as derivatives of azobenzene, t-butylazobenzene or azoxybenzene

PART I: THE ELECTRONIC EFFECT OF THE UNHINDERED AND HINDERED CONFIGURATIONS OF THE AZO AND AZOXY GROUPS

1 INTRODUCTION

1.1 Electrophilic Substitution in Azobenzene

The only electrophilic substitution reactions of azobenzene that have been studied are halogenation, nitration and sulphonation, and early results showed that *para* substitution was favoured. Werner (1899)[10] reported that nitration of azobenzene with nitric acid in acetic acid gave a mixture of the 4-nitro and 4,4'-dinitroazobenzenes together with some 4-nitro-ONN-azoxybenzene. Werigo (1865, 1873)[11] found that 4,4'-dibromoazobenzene resulted from the bromination of azobenzene with neat bromine. Griess (1870)[12] produced a mixture of the 4-substituted and 4,4'-disubstituted sulphonic acids on treating azobenzene with oleum at 170°.

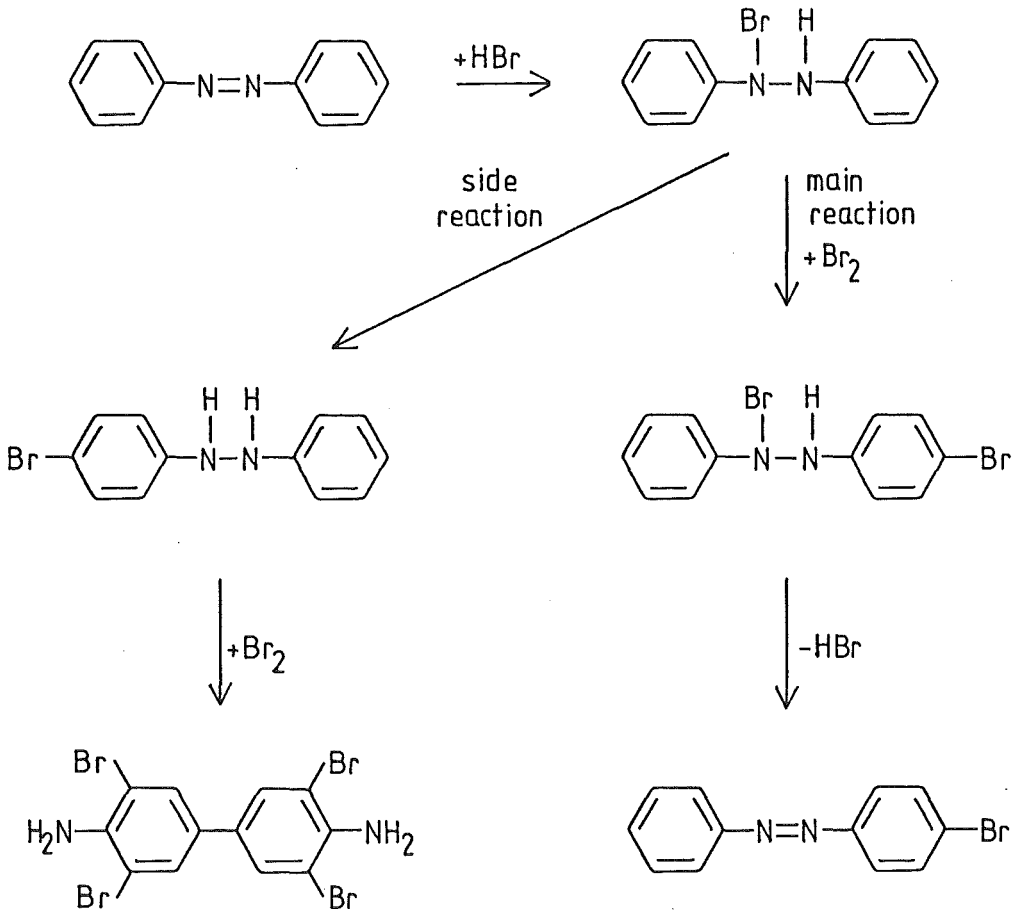
In 1928 Burns, McCombie and Scarborough[13] reported the results obtained on nitration, bromination and chlorination of some monosubstituted azobenzenes and confirmed that substitution at the *para* position is favoured. The 3- and 4-chloroazobenzenes gave only the corresponding 4'-substituted product. Thus 3-chloroazobenzene on treatment with 30% nitric acid gave 3-chloro-4'-nitroazobenzene. For more activated azobenzenes, disubstitution is favoured. Thus 3-methylazobenzene nitrated with concentrated nitric acid gives 3-methyl-4,4'-dinitroazobenzene. Substituted azobenzenes with strongly activating substituents encourage substitution on the same ring as the substituents, followed by attack at the *para* position of the unsubstituted ring. Thus bromination of 4-methoxyazobenzene with bromine and sodium acetate in acetic acid gave

3-bromo-4-methoxyazobenzene and under more vigorous conditions, 4-methoxy-3,4,5'-tribromoazobenzene.

They also observed that 4-methylazobenzene was unreactive towards bromination and nitration using the mild conditions under which the 3-methyl derivative reacted, thus bromination failed with bromine in acetic acid, but proceeded with neat bromine to give 4-bromo-4'-methylazobenzene. In view of the ease of substitution of the other activated derivatives, the unreactive nature of the 4-methyl derivative was a mystery to Burns and co-workers.

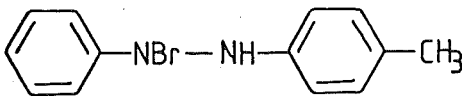
Robertson, Hitchings and Will (1950)[14] attempted to study the kinetics of the bromination of azobenzene using bromine in acetic acid. They observed that a solution of azobenzene and bromine in anhydrous acetic acid did not react when kept at 35° for 16 hours, but on the addition of HBr, reaction occurred. Addition of water to the reaction mixture slowed the reaction and no reaction was observed in 25% aqueous acetic acid. Similar behaviour was observed for chlorination using chlorine in acetic acid, but the addition of water, in contrast to the bromination reaction, increased the reaction rate to one 9 times that of benzene in 20% aqueous acetic acid.

In view of these results, Robertson and co-workers proposed that a special mechanism involving the prior addition of HBr to the azo group was involved. Bromination of the adduct at the position *para* to the NH group then took place, followed by loss of HBr as shown in the scheme over the page.



The side reaction was proposed to explain the reported appearance of the tetrabromobenzidine in the bromination reaction by Mills in 1894.[15]

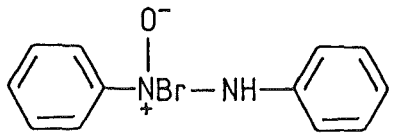
They claimed that this mechanism explained the unreactive nature of 4-methylazobenzene. The adduct (V) would be formed and substitution *para* to the NH group is



(V)

then blocked. Azoxybenzene also displayed the same unreactive nature towards bromine in acetic acid, an observation which led the authors to propose a similar

mechanism with adduct (VI) being the reactive species.



(VI)

The next reported kinetic study was that of Sharnin and Falyakhov[16] (1973) who measured the relative rates of nitration by nitric acid in acetic anhydride at 0° for a series of aromatic compounds. They measured a relative rate of 12.7 for azobenzene in comparison with benzene, which showed the activating nature of the phenylazo group. Their products were the *ortho* and *para*-nitroazobenzenes, formed in a ratio of four to one.

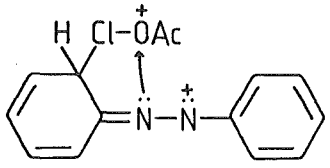
More recently, Miller and co-workers[17] reported that chlorination of azo and azoxybenzene by molecular chlorine in acetic acid did occur in the absence of HCl, and that chlorination with chlorine acetate proceeds much faster than with molecular chlorine. The rate difference observed between the two reagents was of comparable magnitude for benzene and azoxybenzene, but a much larger rate increase for azobenzene was observed. From these results Miller concluded that for chlorination, like nitration, the phenylazo group is *ortho/para* directing and activating, and that in the particular case of molecular chlorination, a special effect is occurring to depress the reaction rate. Such an effect was specific to azobenzene since with azoxybenzene only the expected activation is demonstrated for the two chlorinating reagents.

Miller attributed this lower reactivity of molecular chlorine to the removal of the electrophilic species by complexation of the chlorine with the azobenzene molecule.

They demonstrated this phenomenon by characterizing complexes of molecular bromine and azobenzene.

The interaction of electrophilic species with the azo group to encourage substitution is thought to explain the high *ortho/para* ratios observed in the nitration reaction with nitric acid in acetic anhydride, the chlorination reaction with chlorine acetate, and the exclusive *ortho* attack by mercuric acetate, with azobenzene.[18]

The chlorination reaction using chlorine acetate shows a slight increase in the *ortho/para* ratio (69.6/30.4) to the statistical distribution (66/33), but when the steric effect of the phenylazo group is taken into account, a rate accelerating proximity effect must be involved. Miller suggested this increase in rate may result from stabilization of the transition state VII by the lone electron pair of the adjacent nitrogen.



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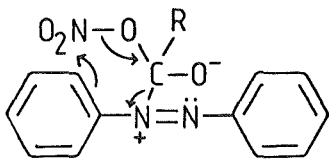

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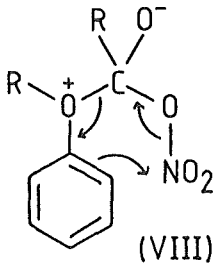
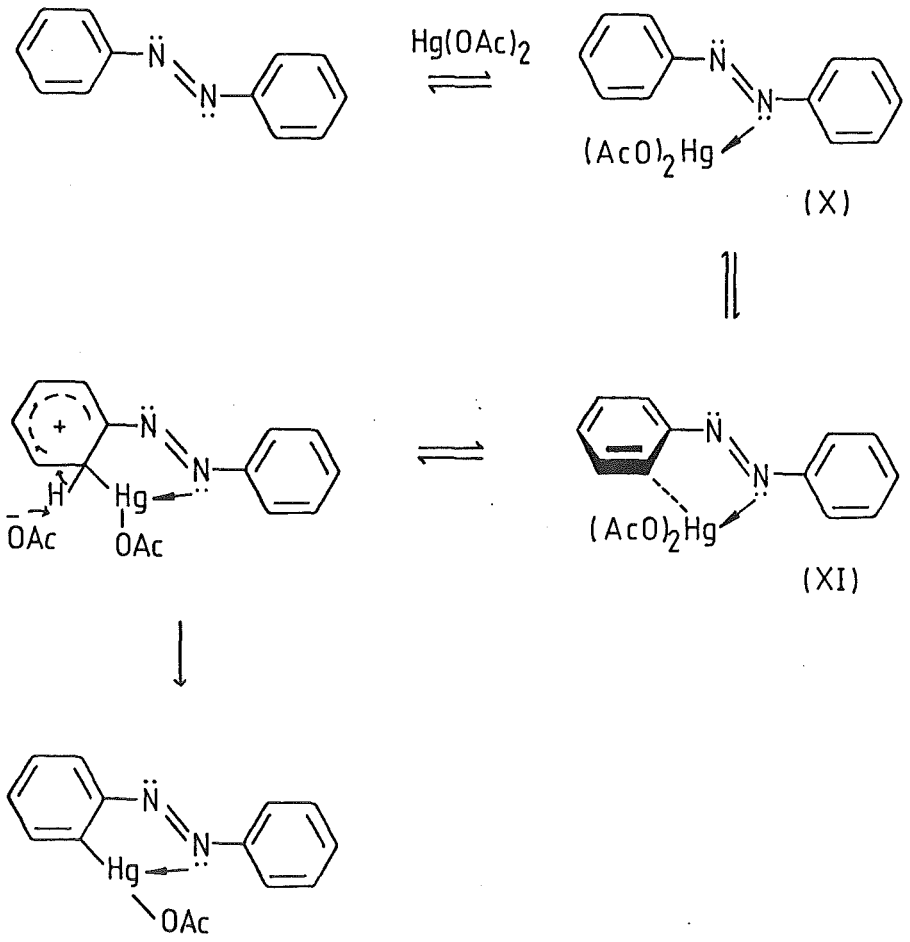


(VIII)

For nitration, a much higher *ortho/para* distribution (79.3/20.7) was observed. The nitration of anisole by nitric acid in acetic anhydride also gives a high *ortho/para* product ratio. A six-centre rearrangement (VIII) has been proposed to explain the high proportion of *ortho* substituted product. Miller has suggested that a similar rearrangement involving the azo group may explain the high *ortho/para* ratio (IX).

Mercuric acetate is not a strong enough electrophile to react at the free *para* position, but coordination of the mercury electrophile to an azo nitrogen lone electron pair (X)

allows the formation of the π-complex (XI), followed by substitution.[18]



This result is not surprising as a number of coordination complexes of azobenzene with transition metals are known.

Finally there has been a recent study of Christoforou performed concurrently with that of Miller of the kinetics of the bromination of azobenzene using $HOBr/HClO_4$ in aqueous dioxan.[19] In this system azobenzene was found to undergo bromination slower than that of benzene by a factor of 4. This is the only reported example of azobenzene behaving as *ortho/para* directing and deactivating.

1.2 The Electronic Effect of the Phenylazo Group

The electronic effect of the phenylazo group as a substituent has not been widely studied. Most of the results that are available are for the side chain reactions of benzene derivatives where the phenylazo group is *meta* or *para* to the side chain. The azo linkage is quite strongly polar and any reactions of *ortho*-substituted analogues would be susceptible to proximity effects.

The first σ value reported for the group was that of +0.64 for *para*-phenylazo proposed by Hammett in 1940 and based on that rate of cleavage of ethylene oxide by phenolate ions. This is presumably a σ^- value. During the last 20 years or so a number of other values have become available.

(i) σ_m and σ_p Values

The reported values of σ_p and σ_m are summarised in Tables 1 and 2 respectively. The results are in general agreement and suggest that the phenylazo group has σ values of around +0.28 (σ_m) and +0.34 (σ_p).

Table 1. Literature σ_m Values for the Phenylazo Group

σ_m	Method	Reference
+0.29	pKa, $ArCO_2H$, 80% methylcellosolve, 25°	20
+0.299	pKa, $ArCO_2H$, 80% methylcellosolve, 25°	21
+0.279	Rate of coupling aryldiazonium salts with R-acid	22
+0.32	Quarter-wave potentials of arylferrocenes, acetonitrile, 25°	23
+0.248	pKa, ArOH, 50% ethanol	20
+0.281	pKa, $ArNH_3^+$, 50% ethanol	20

Table 2. Literature σ_p Values for the Phenylazo Group

σ_p	Method	Reference
+0.33	pKa, $ArCO_2H$, 80% methylcellosolve, 25°	20
+0.349	pKa, $ArCO_2H$, 80% methylcellosolve, 25°	21
+0.31	pKa, $ArCO_2H$, 50% ethanol, 25°	24

(ii) σ^- Values

The reported σ^- values are summarised in Table 3. There is some degree of scatter in the results, which may be

Table 3. Literature σ^- Values for the Phenylazo Group

σ^-	Method	Reference
+0.695	pKa, ArOH, 50% ethanol	20
+0.67-+0.68	^{19}F chemical shifts for *para*-substituted fluorobenzenes	25
+0.672	Rate, 1-chloro-2-nitro-4-X-benzenes with NaOMe/MeOH	26
+0.613	pKa, $ArNH_3^+$, 50% ethanol	20
+0.56	^1H chemical shifts of ArOH, DMSO	27
+0.55	Rate, 1-chloro-2-nitro-4-X-benzenes with piperidine/DMSO	28

due, in part, to the effect of the solvent. For example, the values in DMSO are considerably lower than those in other solvents. A σ^- value of around +0.68 in protic solvents appears to be suggested by the results. The value of 0.613 based on the ionization of anilinium ions in 50% ethanol is therefore surprising as it is difficult to believe that the difference between it and the other values can be due entirely to measurement or extrapolation errors. It may in fact represent some sort of intermediate value between σ and σ^-.

(iii) σ^+ Values

The reported σ^+ values are summarised in Table 4.

Table 4. Literature σ_p^+ Values for the Phenylazo Group

σ_p^+	Method	Reference
-0.4	Rate of chlorination, ClOAc/H^+, 94.7% AcOH-H_2O, 25°	17
-0.37	Rate of coupling aryldiazonium salts with R-acid[A]	22
-0.187	Rate of nitration, HNO_3-Ac_2O, 0°	16
-0.15	Rate of side-chain bromination of toluenes, NBS, benzene	29
-0.12	Rate of chlorination, Cl_2, 80% AcOH-H_2O, 25°[B]	30
-0.04	Rate of chlorination, Cl_2, AcOH, 25°	17
+0.09	Rate of bromination, HOBr/H^+, 75% dioxan-H_2O, 25°	19

[A] Obtained by extrapolation of a σ_p value of +0.190, using the Yukawa-Tsuno equation and an r value of 0.263

[B] Estimated using the rate data of Robertson[30] and assuming the isomer distribution obtained by Miller.[17]

Most of the data are based upon electrophilic substitution rates and should be reasonably reliable as extensive extrapolations of the rate data are not required. The degree of scatter in the σ_p^+ values is therefore difficult to explain since it is much greater than that which could be attributed to experimental error. Such behaviour is not observed for other substituents. It is possible that not all the substitution reactions proceed by the normal mechanism, a point that will be discussed further in the next section. The data do show however that in situations where strongly electron deficient transition states are involved, the phenylazo group is capable of

assisting in the stabilization of the transition state by exerting a significant +R effect. The problem lies in deciding what its true magnitude is. Possible modes of operation of the +R effect will be discussed later, and indeed, investigation of these is one of the main objects of this thesis.

(iv) σ_I Values

The σ_I value for the phenylazo group has only been determined once. Taft and co-workers[31] estimated values of +0.25 in methanol and 0.19 in non-polar solvents (the mean value found in cyclohexane and carbon tetrachloride) based on ^{19}F n.m.r. chemical shift studies of *meta* substituted fluorobenzenes. This value appears to be reasonable when compared with other strong -I -R groups such as acetyl or nitro.

(v) Other σ Values

There have been no substituent constants reported that may be unambiguously assigned as σ° values. The ionization of benzoic acids has been shown (by Wepster[7] and by Taft[6]) to exert a weak demand for π electrons, that is, a weak +R effect. The σ_m and σ_p values for the phenylazo group show that the group is behaving as a -I -R group in this reaction. This implies that it is only likely to become -I +R under conditions where electron demand is very high.

In chemical reactions, transition states stabilised by both +R and -R substituents are very rare and stabilization by having both effects operating

simultaneously has never been proposed. In the benzoic acid ionization reaction, the -R effect of the phenylazo group would contribute nothing to the stabilization of the transition state, but the fact that it is present would not appear to rule out some stabilization by a +R effect. Indeed, since the operation of the -R effect would tend to polarize the molecule and any +R effect would tend to neutralize such polarization the latter should therefore be enhanced.

There are a few other σ_p values that have been reported that tend to fall into an "intermediate" category. These are given in Table 5. The values of 0.39 and 0.37

Table 5. Literature "Intermediate" σ_p Values

"σ_p"	Method	Reference
+0.39	Alkaline hydrolysis of arylacetates, 60% acetone-water	24
+0.37	Alkaline hydrolysis of arylbenzoates, 60% acetone-water	32
+0.44	Basicities of polymethine dyes	33
+0.19	Rate of coupling aryldiazonium salts with R-acid	22

reported by Ryan and Humffray for the alkaline hydrolysis of arylacetates and arylbenzoates respectively are higher than the benzoic acid values, but not by much. For these reactions they estimate Yukawa-Tsuno r values of 0.2 and 0.3 respectively.

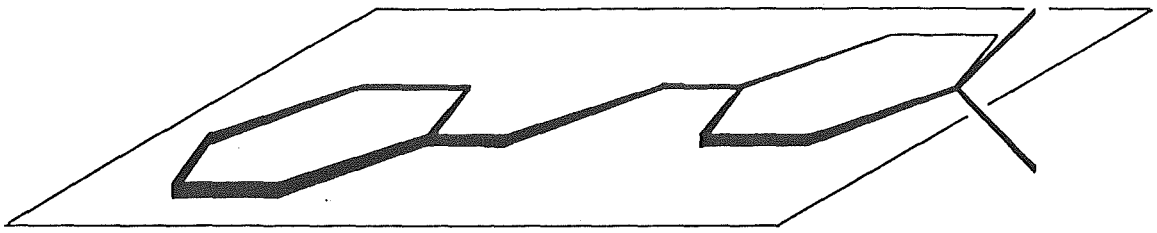
Lifschits and co-workers calculated a value for σ_p of 0.44 for the phenylazo group based on measurements of the basicities of some polymethine dyes.[33] This reaction may have some σ^- component, but judging by the values obtained for other -R groups measured in this system, it should not be large.

The only intermediate value that appears to lie between σ and σ^+ is that reported by Hashida and co-workers,[22] who, based on an investigation of the rates of coupling of diazonium salts with R-acid, reported a value of +0.19. There are some important features of this reaction that are of direct relevance to the work carried out in this thesis, so discussion of the significance of this value will be deferred to later.

1.3 The Influence of Molecular Structure on the Electronic Effect of the Phenylazo Group

A factor that may be related to the variable reactivity of azobenzene towards electrophiles is the geometric relationship between the phenyl rings and the azo linkage. There are four possibilities; these are shown on the following page for the example of the Wheland intermediate formed as a result of attack by an electrophile (X^+) at the *para* position of an azobenzene molecule. Each configuration offers a different mechanism for resonance stabilization of the cationic intermediate.

In (XII) the entire π system is coplanar and so resonance stabilization occurs via the molecule's π system.



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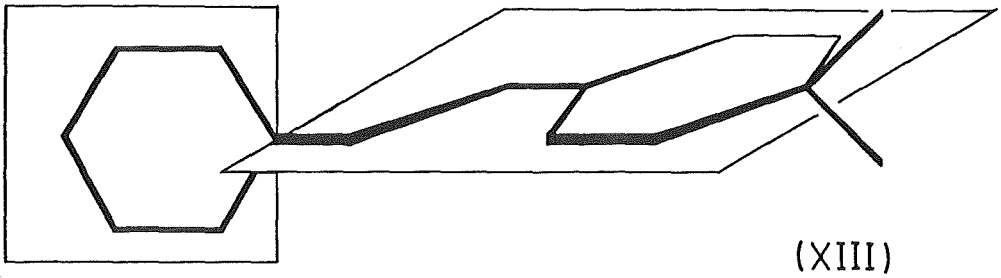

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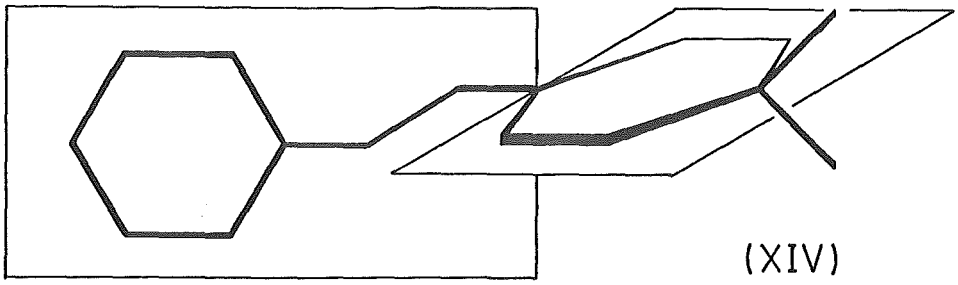
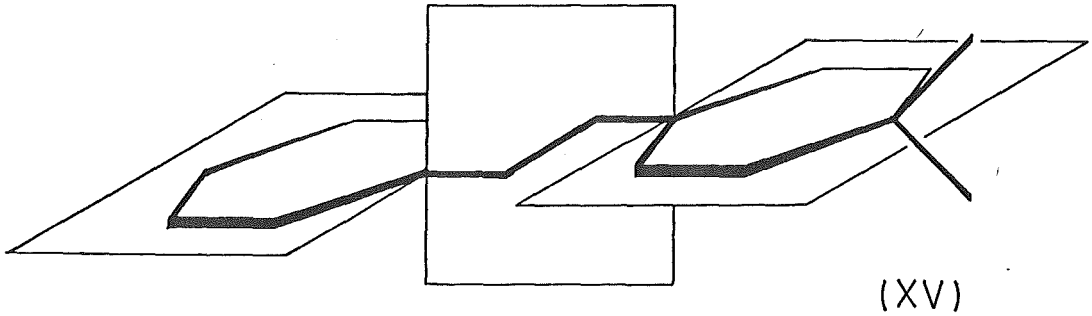
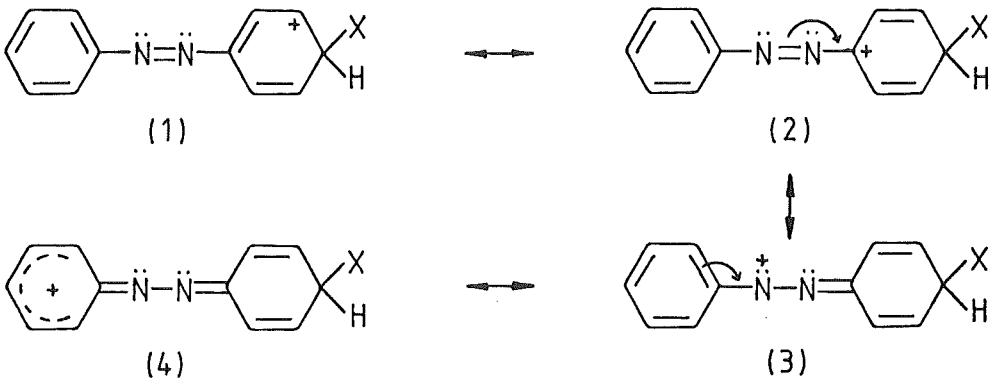


(XIV)



(XV)



(1) (2) (4) (3)

The lone pairs on the azo nitrogens, being orthogonal to the π system, do not play a part in this resonance stabilization.

In (XIII), the unsubstituted phenyl ring (A) is orthogonal to the π system of the azolinkage and ring B. This allows resonance stabilization via forms (1) to (3) but not (4). The destabilization resulting from the loss of form (4) is compounded by the resonance interaction between the π system of ring A and the lone pair on the adjacent nitrogen that is now possible, to give form (5). However

(5)

the contribution of form (5) to the overall resonance scheme is expected to be very small.

In (XIV), the π system of the unsubstituted phenyl ring A and the azo group are coplanar, but orthogonal to, the π system of the ring undergoing attack, B. This means that resonance interaction between the two π systems is no longer possible, thus eliminating resonance forms (3) and (4). But a new resonance form, (6), involving the electron deficient π system of ring B and the lone pair on the adjacent azo nitrogen now becomes possible.

(6)

Stabilization of the intermediate via (6) is potentially much greater than any of the others, since unlike forms (1) to (5) none of the nuclei in (6) are formally π-electron deficient. Furthermore, indirect stabilization involving the orthogonal planar phenylazo π system is also possible.

(7)

In the final possibility, (XV), the π systems of both phenyl rings are orthogonal to the azo π system. This means that it can only be stabilized by form (6), with form (7) being eliminated.

Of the four possible configurations, we would anticipate that (XII) would be favoured over (XIII), and (XIV) would be favoured over (XV). But the difficulty arises in deciding on the relative stability of forms (XII) and (XIV).

Other things being equal, we would expect configuration (XIV) to be the more stable of the two because of its ability to utilize the non-π deficient resonance form (6). However, the azobenzene molecule in solution is thought to exist predominantly as a planar molecule, although there is free rotation around the C-N bond

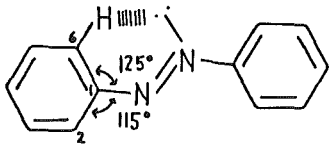
(this will be discussed in greater detail shortly). In the substitution process it is therefore conceivable that the formation of a bond between the phenyl ring and the electrophile initially involves the planar form and that as the reaction progresses, rotation of the azo linkage around the C-N bond occurs. A consequence of this could be that the extent to which this bond rotation has progressed may depend on how early the transition state is reached. An early, reactant-like transition state should resemble (XII) in configuration, whereas a late, product-like transition state could look more like (XIV). It is possible therefore that electrophilic substitution is a reaction where the structure of the substituent is in effect reaction dependent. In such a situation the substituent constant is unlikely to remain constant and this may explain the substantial variations in σ_p^+ values for the phenylazo group.

Distinguishing between the two for the case of azobenzene itself poses a problem. However, if one makes the assumption that for substituted azobenzenes a similar choice of stabilisation mechanisms is offered, then, by making suitable structural variations, it is possible to restrict this choice and, by studying the effect of such changes on the reactivity of the molecule, establish which of the two configurations is the more likely to be involved in the parent molecule.

Ideally, one would wish to obtain models for both situations, i.e. study derivatives where (a) the system is held in a planar configuration and (b) restricted to a non-planar one. The first would seem to require the use of

some form of bridging between the two rings. The second is best achieved by the use of bulky groups in the positions *ortho* to the azo linkage. From a synthetic point of view the first is much the more difficult of the two, so it was decided to concentrate on the latter.

In the solid state, x-ray structural analysis of azobenzene and *para* substituted azobenzenes shows an approximately planar structure.[34] The C2-C1-N and the C6-C1-N angles differ slightly. This is thought to arise from the interaction of the C6-hydrogen with the more distant lone electron pair.

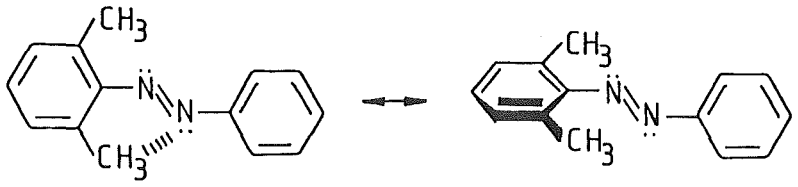


Solid state ^{13}C n.m.r. of azobenzene is also consistent with a planar structure with the C2 and C6 carbons being non-equivalent.[35] However, in solution, the ^{13}C n.m.r. spectrum shows the C2 and C6 carbons to be equivalent, indicating free rotation on the NMR time scale. Similar chemical shifts of the C1 carbon in the solid state and in solution has been put forward as evidence that the equilibrium configuration in the solution phase is not too different from that in the solid state (i.e. 8-12° rotation between the phenyl rings and the azo group), or in the gas phase (about 30° rotation). It must be borne in mind, however, that freedom of rotation around the C-N bonds means that any configuration desired is possible in solution.

There are heterocyclic compounds that give a coplanar configuration of the cis-azo group. These will be discussed later.

The non-planar configuration of azobenzene appears to be difficult to model exactly (except in some cis-azo type heterocycles).

Introduction of substituents into positions *ortho* to the phenylazo group would be expected to make coplanarity more difficult, if not impossible to achieve, and thereby give a structure approximating the non-planar configuration.



There have been a limited number of these "hindered" azobenzenes reported in the literature and study of their properties suggests that some degree of non-planarity is observed.

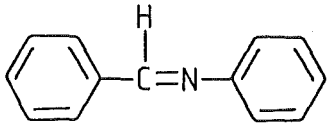
X-ray structural determinations on *ortho* substituted azobenzenes reveal that in many of them crystal packing forces are an important influence on the structure of the molecule, and can compensate for any strain resulting from the forcing of a planar configuration. In some cases however, where large *ortho* substituents are involved they are insufficient. For example, for a series of 2,2',4,4',6,6'-hexaalkylazobenzenes X-ray studies have shown that whereas for the t-butyl[36] and i-propyl[37] derivatives, the molecules are tightly packed, but relatively unstrained, with angles between the planes of the benzene rings of 68.7° and 76.2° respectively, the hexamethyl derivative[38] has a

planar structure, possesses a centre of symmetry and is relatively undistorted.

The solid state ^{13}C n.m.r. spectrum of 2,2',6,6'-tetramethylazobenzene shows non-identical shifts for the C2 and C6 carbons.[35] This is in agreement with the planar X-ray structure of the hexamethyl derivative and is thought to result from the interaction of the lone electron pair on the more distant nitrogen with a methyl group.

In solution, the ^{13}C n.m.r. spectrum shows the C2 and C6 carbons to be equivalent. Theoretical calculations based on the observed electronic spectra suggest that methyl groups in all the *ortho* positions should produce a rotation of 40° between the azo linkage and the phenyl groups.

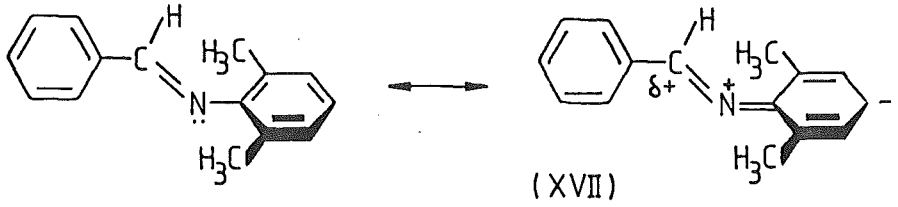
A related system is the N-benzylideneanilines (XVI) where similar steric requirements to the azobenzene molecule can be envisaged to be present. This system has also been studied by various methods.



(XVI)

Gas phase electron diffraction studies[39] have shown that the angle of rotation between the anilino benzene ring and the -CH=N- axis is 52°, with the benzylidene ring lying in the same plane as the -CH=N- group. In the solid state, however, crystal packing forces are thought to be the important factor and a variety of rotation angles are observed with different substituted derivatives.[40] Theoretical calculations based on photoelectron spectra support an approximately 50° rotation angle in the gas phase.[41] In solution, calculations based on the electronic absorption spectra[42] indicate that the angle of rotation is around 30-35°, which, while smaller than in the gas phase, is still far from the non-planar 90°.

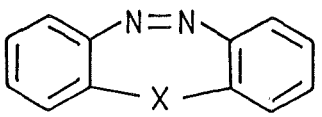
The effect of introducing two *ortho* methyl groups into the anilino ring is believed to give an angle of rotation of 90° since calculations for both the solution and gas phases support a figure around this value. Support for this comes from ^{13}C n.m.r. studies, which show a significant upfield shift in C4 (the *para* carbon on the anilino ring) and a downfield shift in C7 (the C-H carbon) relative to benzylideneaniline itself.[43] This change can be attributed to an increase in electron density at C4 due to the resonance interaction shown in (XVII). The subsequent positive charge on the nitrogen decreases the



(XVII)

electron density at C7 and results in a downfield shift in the resonance position.

There are a number of heterocyclic compounds that are related to cis-azobenzene which induce either a planar or non-planar cis-azo linkage. One example is the series of compounds with different linking groups (X):



(XVIII)= no linking group
(XIX) = $-CH_2-$
(XX) = $-CH_2-CH_2-$

The coplanar azo group is present in (XVIII)(benzocinoline), whereas in (XX), a non-planar azo group is present in a "boat" type molecular configuration.[44] Compound XIX has an intermediate configuration.

In choosing a system to model the non-planar configuration of azobenzene, our choice appears to be limited to heterocyclic compounds or *ortho* substituted azobenzenes. We chose the latter.

The heterocyclic approach was not used, firstly because of the need to compare the result with cis-azobenzene which shows a tendency to isomerise to the more stable *trans* form, and secondly because of the synthetic problems in preparing the appropriate derivatives substituted at the desired position.

A decision was made to use the di-*ortho* methyl substituted azobenzenes since the available literature material indicated that at least some degree of hindrance (non-planarity) should be expected. Although t-butyl substituents would have exerted a greater steric influence than the methyl substituents, we decided on the latter on pragmatic grounds; the preparation of the appropriate precursors has only been reported previously for this case.

It was felt that at the present time, an investigation to determine whether a hindered (non-planar) phenylazo configuration) was more reactive than the unhindered (planar) one was more important than attempting to fully quantify the effect.

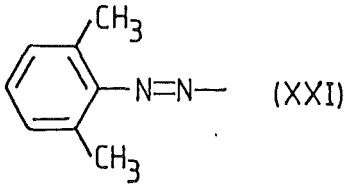
Flanking methyl groups have been used in a similar manner in the past to examine the electronic effects of substituents under steric constraints, especially in situations where the substituent can no longer interact with the aromatic π system by resonance.

Schaefer and Miraglia[45] reported the pKa's of a series of 4-substituted-3,5-dimethylbenzoic acids in 50% ethanol-water. For substituents such as amino, hydroxy, chloro, bromo and cyano the "normal" σ_p values were obtained (after the effect of the dimethyl groups was allowed for). However, for substituents such as dimethylamino, ethoxy, acetamido, carbomethoxy and nitro, the observed σ_p values differed from the normal σ_p values. This was attributed to loss of resonance interaction between the substituent and the π system. For example, the dimethylamino substituent gave a hindered σ_p value of -0.20, much less than the normal σ_p value of -0.83.

Brown and Cleveland[46] reported a similar effect when studying the solvolysis of 4-phenylphenyldimethylcarbinyl chloride. The normal σ_p^+ value (-0.19) of the phenyl group fell to -0.04 (corrected) in the *para*-3,5-dimethylphenyl analogue.

1.4 The Electronic Effect of the 2,6-Dimethylphenylazo Group

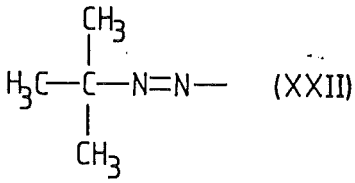
In the 2,6-dimethylphenylazo group (XXI) the two methyl


(XXI)

groups have little influence on the relative configurations of the azo group and the reacting ring. Their influence on the electronic effect of the group will depend rather on the extent to which they force the non-reacting ring out of the plane of the azo group. If they are successful in this regard, then, relative to a phenyl group, the activating power is increased as a result of the introduction of two +I groups, but decreased as a result of the loss of the +R effect of the aromatic nucleus. Of the two, the latter would be expected to be the more important, and the 2,6-dimethylphenylazo group should be less activating than phenylazo. On the other hand, if the system remained planar, or substantially so, the +R effect would be not only retained, but reinforced, making the group more activating than phenylazo.

1.5 The Electronic Effect of the t-Butylazo Group

The t-butylazo group (XXII), was also considered to be worthy of study because of its similarity to azobenzene


(XXII)

and the fact that no Hammett σ values have been reported for this group.

The electronic effect of the non-planar configuration of the t-butylazo group was also of interest because, in contrast to the non-planar phenylazo and 2,6-dimethylphenylazo groups, there are no conformational requirements necessary for the t-butyl group before it will interact by resonance with the non-planar azo group.

1.6 Electronic Effect of the Phenylazoxy Groups

Just as was found to be the case with azobenzenes, the most widely reported electrophilic substitution reactions of azoxybenzene have been nitration and halogenation. Halogenation (bromination and chlorination) takes place at the *para* position furthest from the azoxy oxygen (the 4-position). If this is blocked, then the next most reactive site is the 2-position. Substitution in the ring adjacent to the azoxy oxygen does not appear to be favoured unless it bears strongly activating groups (e.g. hydroxy or ethoxy).

Azoxybenzenes also react at the oxygen. Under strongly acidic conditions azoxybenzene rearranges to 4-hydroxyazobenzene via the Wallach rearrangement.[47] Deoxygenation to azo compounds is achieved by both acid halides and aluminium halides.[48] All of these reactions placed limitations on attempts to study electrophilic substitution in azoxybenzenes, and because of difficulties in separating and identifying the azoxybenzene isomers, the amount of quantitative data on the phenylazoxy substituent is very small.

There have only been a small number of Hammett substituent constants reported for the two groups. Values that

should represent σ^- ones have been determined for both groups based on the basicities of the corresponding dimethylaminoazoxybenzenes in 20% ethanol,[49] and on the rates of reaction of 1-chloro-2-nitrobenzenes with sodium methoxide in methanol.[26] For the phenyl-ONN-azoxy group, values of +0.56 and +0.62 respectively were found. The isomeric phenyl-NNO-azoxy group gave respective values of +0.78 and +0.77.

These figures suggest that both azoxy groups are -I -R in character. On this basis, *meta* substitution with electrophiles would be expected, so the experimentally determined *ortho/para* directing nature indicates a potential +R character for the phenyl-ONN-azoxy group. Only one estimate of σ_p^+ has been reported, that of -0.04 by Christoforou based on the kinetics of positive bromination with hypobromous acid in 75% dioxan-water.[50b] Miller and coworkers have measured the rates of chlorination of azoxybenzene with both chlorine in acetic acid and chlorine acetate in 94.7% acetic acid, but they reported no product distributions. The assumption of a similar product distribution to that recorded by Christoforou (i.e. 50% para product), lead to a σ_p^+ value of about -0.2 for chlorination in acetic acid and -0.3 for chlorination using chlorine acetate. These values all confirm the +R character of the phenyl-ONN-azoxy group.

Again, a range of σ_p^+ values appears to be applicable to the phenyl-ONN-azoxy group, although the variation does not appear to be as great as that observed for the phenylazo group. It is conceivable that similar influences are operating in both systems.

There have been no previously reported σ_I, σ^o, σ_m or σ_p values for either substituent.

The +R character of the phenyl-ONN-azoxy group is thought to result from the increased stabilization of the Wheland intermediate by the resonance form (XXIII) in the coplanar intermediate.

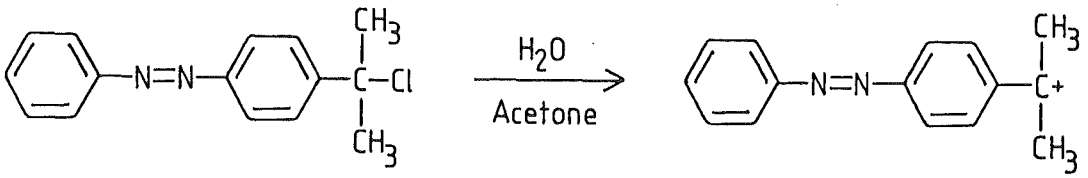
(XXIII)

For the phenyl-NNO-azoxy substituent, no such stabilization mechanism is possible. Its structure in fact resembles that of a nitro group.

1.7 An Outline of the Approach Pursued

Since our survey of the literature revealed that electrophilic substitution in azobenzenes is unusual in that it produces a wide range of σ_p^+ values for the phenylazo group, behaviour not generally observed for other substituents, a further investigation into the electronic properties of the phenylazo group, and factors that may have an influence upon them was considered to be warranted.

In the first instance it was decided to determine the σ_p^+ value using the classical method of Brown, the solvolysis of 4-phenylazophenyldimethylcarbinyl chloride in aqueous acetone, which proceeds via the cationic intermediate:



This should yield a value of σ_p^+ that would be expected for an electrophilic substitution reaction free from mechanistic complications.

The result obtained, however, was sufficiently unusual that it was clear that the reason for the variable σ_p^+ values obtained probably lay in the mechanism of resonance stabilization rather than in the mechanism of substitution. Most of the rest of our investigation followed from attempts to elucidate this. Since it seemed likely that variations in the geometry of the phenylazo substituent could be involved, attempts were made to modify this by the use of substituents.

Firstly, two methyl groups were introduced into positions *ortho* to the azo linkage and their effect on the electronic effect of the azo function was investigated by establishing the effect on both the pKa's of benzoic acids and on the carbinyl chloride solvolysis rates. These groups were considered likely to force some degree of non-planarity between the phenylazo group and the phenyl ring bearing the reaction site. This data, after correcting for the presence of the methyl groups, gave "hindered" σ_p and σ_p^+ values for the phenylazo group.

The effect of hindrance to coplanarity of the non-reacting phenyl group was also investigated using the same technique by measuring the σ_p^+ value for the 2,6-

dimethylphenylazo group in both the unhindered and hindered configurations.

Secondly, electronic effects of the t-butylazo, phenyl-ONN-azoxy and phenyl-NNO-azoxy groups were studied by the same method. These were in fact considered worthy of study in their own right, since they had received no attention previously, but in our case they also were capable of yielding information, since they can be considered as "modified" (indeed extremely so) versions of phenylazo. The effect of systematically modifying the group by introducing substituents in the far ring was also briefly studied.

EXPERIMENTAL

2.0 General Introduction

All solvents used, (except those used in the measurement of the solvolysis rates) were technical grade. Petroleum ether was distilled before use. Diethyl ether (hereafter referred to as "ether") used in chromatography and as anhydrous ether in synthesis, was dried over anhydrous calcium chloride then stored over sodium wire. Tetrahydrofuran (THF) was refluxed and distilled from calcium hydride immediately before use. Dichloromethane for use in the phenyldimethylcarbinyl chloride synthesis and recrystallizations, was distilled twice from phosphorus pentoxide. All other solvents were used without further purification.

Commercially available reagents were used without further purification, as were compounds prepared previously within the department, unless stated otherwise.

Laporte type H 100-200 mesh alumina and silica gel grade 923 were used for column chromatography. Small scale preparative chromatography was carried out on a Chromatotron (a centrifugally accelerated, radial thin layer chromatograph), model 7924, Harrison Research Inc. The Chromatotron rotors were coated with silica gel (PF 254 type 60, Merck:EM Laboratories Inc.) unless stated otherwise,and of two millimetre thickness. Compounds were eluted with ether/ petroleum ether mixtures and non-coloured compounds were visualised under ultraviolet light.

Proton NMR spectra were recorded on a Varian T-60 or Varian EM360 60MHz spectrometer, and were recorded for samples dissolved in either carbon tetrachloride or

deuterochlorofrom with tetramethylsilane as an internal standard.

Carbon-13 NMR spectra were obtained on a Varian CFT-20 NMR spectrometer operating at 22 MHz with a probe temperature of 33°C. All spectra were recorded in deuterochloroform.

Infrared spectra were recorded on either a Shimadzu IR-27G or Pye Unicam SP3-300 spectrometer.

The molecular formulae of compounds not previously reported in the literature were confirmed by microanalysis, which was carried out at the University of Otago. If this failed, exact mass determinations were made using an AEI MS 902 mass spectrometer.

Melting points were determined in an open-top capillary and were uncorrected.

Small scale distillations were carried out in a Kugelrohr apparatus (Buchi GKR-50).

A full list of the carbon-13 n.m.r. chemical shifts for the azobenzenes, t-butylazobenzenes and the azoxybenzenes prepared in Part I are listed in the Appendix.

Most of the azobenzenes and azoxybenzenes were prepared by the same general methods. These are given below.

General Procedure for the Preparation of Azobenzenes

Equimolar quantities of the nitrosobenzene and the aniline were dissolved in acetic acid (5 ml/g) and heated on a steam bath for 4 h. The solution was then cooled, diluted with water and extracted with dichloromethane. The extract was added to water and solid sodium bicarbonate was cautiously

added until the effervescence ceased. The extract was then separated, washed with water, dried over magnesium sulphate and the solvent removed under reduced pressure. The residue was dissolved in a minimum amount of benzene, adsorbed onto an alumina chromatographic column, and the azobenzene eluted with light petroleum/dichloromethane. This product was further purified by means of the Chromatotron and finally recrystallized from ethanol.

General Procedure for the Oxidation of Azobenzenes to Azoxybenzenes

To a solution of the azobenzene in acetic acid (5 ml/g), 30% hydrogen peroxide (10% of the acetic acid volume) was added and the solution heated on a steam bath for 2-3 h. During this time a further volume of hydrogen peroxide (5% of the acetic acid volume) was added. The yellow solution was worked up in a manner similar to that described for the preparation of azobenzenes and the crude azoxybenzene mixture was purified by chromatography using an alumina chromatographic column. This yielded a mixture of the two azoxybenzenes.

2.1 Preparation of the Substituted Benzoic Acids

2.11 Preparation of the Phenylazo Substituted Benzoic and Phenylacetic Acids

The azobenzene esters were prepared by condensation of the appropriate aminobenzoate with nitrosobenzene. After purification, the ester was hydrolysed with potassium hydroxide in ethanol. The hydrolysis procedure is described in detail for the preparation of 3-phenylazobenzoic acid. The same method is used throughout this thesis.

3-Phenylazobenzoic Acid

(i) Nitrosobenzene

This was prepared by reducing nitrobenzene with zinc powder in aqueous ammonium chloride solution followed by dichromate oxidation, as described in Vogel.[51] The crude product was freed from inorganic material by dissolving the product in ether, the ether solution was washed with water, dried with magnesium sulphate, and the solvent removed under reduced pressure. The nitrosobenzene was stored under refrigeration.

(ii) Methyl 3-Phenylazobenzoate

Methyl 3-aminobenzoate and nitrosobenzene were condensed in the normal manner and purified on a silica Chromatotron plate to give methyl 3-phenylazobenzoate (44% yield), m.p. 58.5-60° (lit. 57-58°[52]). ν_{max} (Nujol) 1735 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 3.97, CH_3; 7.43-8.27, m, 9H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 52.3, CH_3; 122.9, C1; 123.0, C2'; 124.0, C2; 126.9, C4; 129.1, C3', C5; 131.4, C4'; 131.6, C6; 152.5, C1'; 152.6, C3; 166.5, C=O.

(iii) 3-Phenylazobenzoic acid

A solution of methyl 3-phenylazobenzoate (0.50 g) in ethanol (15 ml) and potassium hydroxide (0.18 g) was refluxed for 1 h. The solvent was then removed under reduced pressure, water (100 ml) was added and the resulting solution washed with ether. After separation of the ether layer, the aqueous phase was acidified with 5% sulphuric acid. The crude acid that precipitated was filtered off and dissolved in ether (150 ml). The ether solution was washed with water, dried over sodium sulphate and the ether evaporated. The orange solid obtained was recrystallised from ethanol to give 3-phenylazobenzoic acid (0.34 g), m.p. 165-166° (lit. 166-167°[52]). ν_{max} (Nujol) 1675 cm^{-1}, C=O.

4-Phenylazobenzoic Acid

(i) Ethyl 4-Phenylazobenzoate

Ethyl 4-aminobenzoate and nitrosobenzene were condensed in the normal manner and purified on a silica Chromatotron plate to give ethyl 4-phenylazobenzoate (43% yield), m.p. 81.5-82° (lit. 85-86°[53]). ν_{max} (Nujol) 1725 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 1.43, t, J7Hz, CH_3; 4.47, q, J7Hz, CH_2; 7.52-7.70, m, 3H, phenyl protons; 7.92-8.38, m, 6H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.3, CH_3; 61.2, CH_2; 122.6, C2'; 123.2, C3; 129.2 C3'; 130.6, C2; 131.6, C4'; 132.2, C1; 152.6, C1'; 155.1, C4; 166.0, C=O.

(ii) 4-Phenylazobenzoic Acid

Ethyl 4-phenylazobenzoate (0.62 g) was hydrolysed with potassium hydroxide in ethanol to give 4-phenylazobenzoic acid (0.41 g), m.p. 233-235° (lit. 204°[54]). ν_{max} (Nujol) 1685 cm^{-1}, C=O.

4-Phenylazophenylacetic Acid

(i) Ethyl 4-Phenylazophenylacetate

Ethyl 4-aminophenylacetate (2.88 g) and nitrosobenzene (2.0 g) were condensed in acetic acid in the normal manner to give ethyl 4-phenylazophenylacetate (2.57 g) as an orange solid. ^{1}H n.m.r. (CCl_4) δ 1.25, t, J7Hz, CH_3; 3.58, CH_2; 4.10, q, J7Hz, CH_2-Me; 7.25-7.50, m, 5H, phenyl protons; 7.75-8.00, m, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.2, CH_3; 42.3, CH_2CO; 61.6, CH_2Me; 122.8, C2'; 123.1, C3; 129.1, C3'; 130.0, C2; 131.0, C4'; 137.2, C1; 151.8, C4; 152.7, C1'; 171.1, C=O.

(ii) Phenylazophenylacetic Acid

Ethyl 4-phenylazophenylacetate (0.40 g) was hydrolysed with potassium hydroxide in ethanol to give 4-phenylazophenylacetic acid (0.23 g), m.p. 196-197° (Found C, 69.9; H, 5.2; N, 11.6. $C_{14}H_{12}N_2O_2$ requires C, 70.0; H, 5.0; N, 11.7%). ν_{max} (Nujol) 1700 cm^{-1}, C=O.

3,5-Dimethyl-4-phenylazobenzoic Acid

This compound was synthesized by the condensation of ethyl 4-amino-3,5-dimethylbenzoate, prepared from mesitylene by the method given below, with nitrosobenzene to give ethyl 3,5-dimethyl-4-phenylazobenzoate. Subsequent hydrolysis gave the acid.

(i) Nitromesitylene

Mesitylene (45 g) was nitrated with fuming nitric acid in acetic anhydride by the method described by Powell and Johnson[55] to give nitromesitylene (27.5 g).

(ii) 3,5-Dimethyl-4-nitrobenzoic Acid

The nitromesitylene obtain in the previous reaction was treated with chromium trioxide in acetic acid,[56] to give 3,5-dimethyl-4-nitrobenzoic acid (21.4 g), m.p. 213-218° (lit. 214-215°[56]).

(iii) Ethyl 3,5-Dimethyl-4-nitrobenzoate

3,5-Dimethyl-4-nitrobenzoic acid (21 g) was esterified with ethanol (100 ml) and concentrated sulphuric acid (2.5 ml) to give ethyl 3,5-dimethyl-4-nitrobenzoate (12.3 g), m.p. 66° (lit. 72°[57]).

(iv) Ethyl 4-Amino-3,5-dimethylbenzoate

Ethyl 3,5-dimethyl-4-nitrobenzoate (5.62 g), dissolved in ethanol (200 ml), was hydrogenated in a Parr apparatus at 40-50 p.s.i. using 5% Pd/C catalyst to give ethyl 4-amino-3,5-dimethylbenzoate (4.2 g), m.p. 64-65° (lit. 67°[58]).

(v) Ethyl 3,5-Dimethyl-4-phenylazobenzoate

Ethyl 4-amino-3,5-dimethylbenzoate (4.2 g) and nitrosobenzene (2.3 g) were condensed in the normal manner to give ethyl 3,5-dimethyl-4-phenylazobenzoate (3.2 g), m.p. 65.6-67°. ν_{max} (liquid film) 3000, CH; 1725 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.40, t, J7Hz, CH_3; 2.37, Me_2; 4.30, q, J7Hz, CH_2; 7.33-7.58, m, 3H, phenyl protons; 7.72, H2, H6; 7.75-8.00, m, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.4, CH_3; 18.4, Me_2; 60.9, CH_2; 122.7, C2'; 129.2, C3'; 130.1, C3; 130.3, C2; 131.6, C4'; 152.7, C1'; 155.0, C4; 166.3, C=O; n.o. C1.

(vi) 3,5-Dimethyl-4-phenylazobenzoic Acid

Ethyl 3,5-dimethyl-4-phenylazobenzoate (1.07 g) was hydrolysed with potassium hydroxide in ethanol to give 3,5-dimethyl-4-phenylazobenzoic acid (0.44 g), m.p. 195-197° (Found C, 71.0; H, 5.8; N, 11.1. $C_{15}H_{14}N_2O_2$ requires C, 70.9; H, 5.6; N, 11.0%). ν_{max} (Nujol) 1690 cm^{-1}, C=O.

2.12 Preparation of the t-Butylazobenzoic Acids

The methods described in the literature for the preparation of alkylazobenzenes or alkylazoxybenzenes fall into two groups.

The first involves the action of alkyl Grignard reagents with phenyldiazonium fluoroborates to give the alkylazobenzene. For example:[59]

$$RMgX + PhN_2^+ \longrightarrow RN{=}NPh \qquad (\sim 50\%)$$

In the second a nitrosobenzene is treated with an alkylamine under oxidising conditions to form the alkylazoxybenzene. For example the method of Barton:[60]

$$RNH_2 + PhNO + I_2/Bu^tOCl \longrightarrow RN{=}\overset{+}{N}(O^-)Ph \qquad (\sim 90\%)$$

Work has also been reported on a similar reaction using a different medium giving similar yields.[61]

We required a method that allowed the formation of a t-butylazobenzene where an acid derivative (hopefully an ester) was already present on the phenyl group. Because the first method involves the action of Grignard reagents with which acid derivatives were incompatible, it could not be

used, (also the low reported yields made it unattractive). We chose the method of Barton because of its high yields and the relative ease of preparing the 3-and 4-nitrosobenzoates. Reduction of the azoxy group to the azo group was achieved by initial reduction to the hydrazo derivative with zinc dust in ethanolic acetic acid, followed by oxidation with yellow mercuric oxide.

Purification of the nitrosobenzoates was usually not attempted as it was found to be easier to purify the t-butyl-azoxybenzoates instead.

4-t-Butylazobenzoic Acid

(i) Ethyl 4-Nitrosobenzoate

Ethyl 4-nitrobenzoate was reduced by the method of Hall and Dolan[62] to give a cream solid, shown (by ^{1}H n.m.r.) to be 70% ethyl 4-nitrosobenzoate. It was normally used without further purification.

A small sample of the crude material (0.65 g) was adsorbed onto a silica/polyethylene glycol Chromatotron plate and elution with light petroleum gave ethyl 4-nitroso-benzoate (0.25 g), m.p. 79° (lit. 81°[63]).

(ii) Ethyl 4-t-Butyl-NNO-azoxybenzoate

To a solution of crude ethyl 4-nitrosobenzoate (8.3 g) in benzene (450 ml) was added t-butylamine (3.2 g), iodine (27 g) and t-butyl hypochlorite (12.5 ml). The solution was stirred overnight, then washed repeatedly with aqueous sodium thiosulphate until the iodine colour was discharged, dried with magnesium sulphate and the solvent evaporated under reduced pressure to give a dark oil. This crude ethyl

4-t-butyl-NNO-azoxybenzoate was used in the next step without further purification. ^{1}H n.m.r. (CCl_4) δ 1.38, t, J7Hz, CH_3; 1.45, Me_3; 4.35, q, J7Hz, CH_2; 8.10, 4H, phenyl protons.

(iii) Ethyl 4-t-Butylazobenzoate

A solution of the crude ethyl 4-t-butyl-NNO-azoxybenzoate from the previous step in ethanol (100 ml) and acetic acid (10 ml), was heated to 70° and zinc dust (14 g) was carefully added. The mixture was allowed to stand for 5 min, then the zinc salts were filtered off and the filtrate was added to water. The mixture was extracted with dichloromethane, the dichloromethane solution dried with magnesium sulphate and the solvent removed under reduced pressure. The residue was dissolved in ethanol (100 ml), yellow mercuric oxide (15 g) was added, and the mixture first heated to reflux for 45 min then stirred overnight at 20°. The mercury salts were filtered off and washed with ether. The combined filtrate and washings were diluted with water, the ether fraction was separated, dried with magnesium sulphate and evaporated. The oily residue was filtered, washed several times with pentane, the filtrate was evaporated to give a dark oil. This material was purified on a silica gel chromatographic column to give ethyl 4-t-butylazobenzoate (3.52 g) as an oil. ν_{max} (liquid film) 3000, CH; 1725 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 1.38, Me_3; 1.42, t, J7Hz, CH_3; 4.40, q, J7Hz, CH_2; 7.70, 8.22, J_{AB} 9Hz, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.3, CH_3; 26.9, Me_3; 61.1, CH_2; 68.5, $\underline{C}Me_3$; 121.7, C3; 130.5, C2; 131.5, C1; 155.0, C4; 166.1, C=O.

(iv) 4-t-Butylazobenzoic Acid

Ethyl 4-t-butylazobenzoate (0.88 g) was hydrolysed with

potassium hydroxide in ethanol to give 4-t-butylazobenzoic acid (0.45 g), m.p. 183-184° (Found C, 64.3; H, 6.8; N, 13.7. $C_{11}H_{14}N_2O_2$ requires C, 64.1; H, 6.8; N, 13.6%). ν_{max} (Nujol) 1690 cm^{-1}, C=O. ^1H n.m.r. ($CDCl_3$) δ 1.38, Me_3; 7.74, 8.22, J_{AB} 9Hz, 4H, phenyl protons; 11.20, bs, OH. ^{13}C n.m.r. ($CDCl_3$) δ 26.9, Me_3; 68.7, $\underline{C}Me_3$; 121.9, C3; 130.2, C1; 131.3, C2; 155.8, C4; 171.9, C=O.

3-t-Butylazobenzoic Acid

(i) Methyl 3-Nitrosobenzoate

The crude material obtained from the reduction of methyl 3-nitrobenzoate (1 g) by the method of Entwistle et.al.,[64] was adsorbed onto a silica Chromatotron plate. Elution with light petroleum gave a yellow solid (0.22 g) shown (^{13}C n.m.r.) to be 65% methyl 3-nitrosobenzoate. It was used in the next step without further purification.

(ii) Methyl 3-t-Butyl-NNO-azoxybenzoate

Methyl 3-nitrosobenzoate (0.80 g) and t-butylamine (0.42 g) were condensed by the method used for the 4-nitroso derivative to give methyl 3-t-butyl-NNO-azoxybenzoate as a yellow oil. ν_{max} (liquid film) 3000, CH; 1730 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 1.47, Me_3; 3.93, CH_3; 7.33-8.75, m, 4H, phenyl protons.

(iii) Methyl 3-t-Butylazobenzoate

Methyl 3-t-butyl-NNO-azoxybenzoate was reduced by the method described for the 4-derivative to give methyl 3-t-butylazobenzoate (0.49 g) as a yellow oil. ν_{max} (liquid film) 3000, CH; 1730 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 1.35, Me_3;

3.90, CH_3; 7.33-8.33, m, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ27.0, Me_3; 52.2, CH_3; 68.1, $\underline{C}Me_3$; 123.3, C2; 126.1, C4; 129.0, C5; 130.8, C6; 131.2, C1; 152.5, C3, 166.6, C=O.

(iv) 3-t-Butylazobenzoic Acid

Methyl 3-t-butylazobenzoate (0.49 g) was hydrolysed with potassium hydroxide in ethanol to give 3-t-butylazobenzoic acid (0.26 g), m.p. 130-131° (Found C, 63.9; H, 7.00; N, 13.7. $C_{11}H_{14}N_2O_2$ requires C, 64.1; H, 6.9; N, 13.6%). ν_{max} (Nujol) 1695 cm^{-1}, C=O. ^1H n.m.r. ($CDCl_3$) δ1.38, Me_3; 7.33-8.40, m, 4H, phenyl protons; 11.00, bs, OH. ^{13}C n.m.r. ($CDCl_3$) δ 25.3, Me_3; 66.7, $\underline{C}Me_3$; 122.4, C2; 125.3, C4; 127.5, C5; 128.6, C1; 129.7, C6; 150.9, C3; 170.3, C=O.

4-t-Butylazo-3,5-dimethylbenzoic Acid

Ethyl 3,5-dimethyl-4-nitrobenzoate was reduced by the action of zinc dust in aqueous ammonium chloride and 2-methoxyethanol to the hydroxylamine, which was then oxidised to the corresponding nitroso compound by ferric chloride. The nitroso compound was reacted with t-butylamine to give the t-butylazoxybenzene, which was subsequently reduced to the t-butylazobenzene by the method described for ethyl 4-t-butylazobenzoate.

(i) Ethyl 3,5-Dimethyl-4-nitrosobenzoate

To a stirred solution of ethyl 3,5-dimethyl-4-nitrobenzoate (1.03 g) in 2-methoxyethanol (13 ml), a solution of ammonium chloride (0.34 g) in water (2.7 ml) was added at 50°. Zinc dust (0.72 g) was then added in small portions over 5 min and the mixture stirred at 50-60° for 1 h. The zinc salts were filtered, washed with warm ethanol (2 ml) and the filtrate

added to an ice-cold stirred solution of hydrated ferric chloride (1.5 g) in water (30 ml) and ethanol (10 ml). After 1 h. the product was extracted with dichloromethane, the solution washed with water, dried with magnesium sulphate and the solvent evaporated under reduced pressure to give a cream solid. This material was washed with dry ether (10 ml) to give ethyl 3,5-dimethyl-4-nitrosobenzoate (0.50 g), m.p. 151-152°. ν_{max} (Nujol) 1720 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 1.37, t, J7Hz, CH_3; 2.47, Me_2; 4.33, q, J7Hz, CH_2; 7.77, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.3, CH_3; 18.7, Me_2; 61.5, CH_2; 130.3, C2; 132.3, C1; 133.5, C3, 144.0, C4; 166.4, C=O.

(ii) Ethyl 4-t-Butyl-NNO-azoxy-3,5-dimethylbenzoate

Ethyl 3,5-dimethyl-4-nitrosobenzoate (2.55 g) and t-butylamine (0.90 g) were condensed in the manner described previously to give ethyl 4-t-butyl-NNO-azoxy-3,5-dimethylbenzoate (3.14 g), m.p. 55-57°. ν_{max} (Nujol) 1730 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.35, t, J7Hz, CH_3; 1.45, Me_3; 2.27, Me_2; 4.32, q, J7Hz, CH_2; 7.65, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.3, CH_3; 16.3, Me_2; 25.7, Me_3; 60.0, $\underline{C}Me_3$; 61.2, CH_2; 128.3, C3; 130.0, C2; 130.1, C1; 165.7, C=O; n.o. C4.

(iii) Ethyl 4-t-Butylazo-3,5-dimethylbenzoate

Ethyl 4-t-butyl-NNO-azoxy-3,5-dimethylbenzoate (3.14 g) was reduced by the method described previously to give ethyl 4-t-butylazo-3,5-dimethylbenzoate (1.10 g) as a yellow oil. ν_{max} (liquid film) 3020, CH; 1725 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.33, Me_3; 1.35, t, J7Hz, CH_3; 2.10, Me_2; 4.22, q, J7Hz, CH_2; 7.58, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.4, CH_3; 17.4, Me_2; 26.9, Me_3; 60.9, CH_2; 69.9, $\underline{C}Me_3$; 128.0, C3; 128.3, C1; 130.1, C2; n.o. C4, C=O

(iv) 4-t-Butylazo-3,5-dimethylbenzoic Acid

Ethyl 4-t-butylazo-3,5-dimethylbenzoate (0.56 g) was hydrolysed with potassium hydroxide in ethanol to give 4-t-butylazo-3,5-dimethylbenzoic acid (0.36 g), m.p. 207-209° (Found C,66.5; H, 8.1; N, 11.7. $C_{13}H_{18}N_2O_2$ requires C 66.6; H, 7.7; N, 12.0%). ν_{max} (Nujol) 1685 cm^{-1}, C=O. ^1H n.m.r. ($CDCl_3$) δ 1.40, Me_3; 2.12, Me_2; 7.75, 3H, phenyl protons and OH. ^{13}C n.m.r. ($CDCl_3$) δ 17.4, Me_2; 26.9, Me_3; 70.0, $\underline{C}Me_3$; 128.1, C3; 130.6, C1; 130.8, C2; 156.6, C4; 172.0, C=O

2.13 Preparation of the Phenylazoxybenzoic Acids

There are three reported methods for the preparation of isomerically pure substituted azoxybenzenes. The first involves the reaction of a Grignard reagent with a substituted N-nitrosohydroxylamine derivative:[65]

$$Ar\overset{+}{N}(O^-)=NOTs + A'rMgX \longrightarrow Ar\overset{+}{N}(O^-)=NA'r$$

In the second a nitrobenzene is condensed with an aryliminodimagnesium reagent:[66]

$$PhNO_2 + ArN(MgBr)_2 \longrightarrow Ph\overset{+}{N}(O^-)=NAr$$

The third is the selective electrophilic substitution of azoxybenzene, for example, bromination.[67]

$$Ph\overset{+}{N}(O^-)=NPh + Br_2 \longrightarrow Ph\overset{+}{N}(O^-)=NC_6H_4Br$$

Attempts to prepare the 4-methylazoxybenzenes by the first two methods failed. The lack of reported use of these methods

suggests that these methods may not have proved as successful as their authors had hoped.

The traditional preparative methods involve the separation of an isomeric mixture of the substituted azoxybenzene into its components. The isomeric mixture is commonly prepared by either the oxidation of azobenzenes or the condensation of phenylhydroxylamines with nitrosobenzenes. Separation of the isomers has often proved difficult, chromatographic techniques generally failing, but there are several reported examples where fractional crystallization is successful.

Both the separation technique and the selective bromination of azoxybenzene were used to prepare the isomerically pure phenylazoxybenzoic acids.

The identification of the isomeric composition of azoxybenzene samples, formerly difficult, has been simplified by the advent of carbon-13 n.m.r. spectroscopy. The alkyl substituted azoxybenzenes, including esters, can also be distinguished by their proton-n.m.r. spectra in benzene. Here the signals due to the alkyl groups are split into two signals with typically 2-6 Hz splitting. The relative heights of these two signals gives an approximate indication of the isomeric composition of the sample, although, unlike ^{13}C n.m.r., one cannot tell which isomer is which.

Preparation of 3-Phenyl-ONN- and 3 -Phenyl-NNO- azoxybenzoic Acids

Oxidation of ethyl 3-phenylazobenzoate with H_2O_2/AcOH

gave a mixture of the two isomeric azoxybenzenes. The mixture was resolved into its components by a combination of crystallization from ethanol and chromatography.

3-Phenyl-ONN-azoxybenzoic Acid

(i) Ethyl 3-Phenylazobenzoate

Nitrosobenzene (2 g) and ethyl 3-aminobenzoate (3 g) were condensed in acetic acid in the normal manner to give ethyl 3-phenylazobenzoate (3.2 g) as a dark red oil (lit. m.p. 36°.[68]).

(ii) Ethyl 3-Phenylazoxybenzoate

Ethyl 3-phenylazobenzoate was oxidised with 30% hydrogen peroxide in acetic acid in the normal manner to give the isomeric mixture of ethyl 3-phenylazoxybenzoates as an oily-solid material.

(iii) Ethyl 3-Phenyl-ONN-azoxybenzoate

Crystallization of the mixture of ethyl 3-phenylazoxybenzoates from ethanol gave pure ethyl 3-phenyl-ONN-azoxybenzoate as pale yellow crystals, m.p. 83°. ν_{max} (Nujol) 1725 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.42, t, J7Hz, CH_3; 4.38, q, J7Hz, CH_2; 7.32-7.57, phenyl protons, 4H; 7.90-8.56, phenyl protons, 5H. ^{13}C n.m.r. ($CDCl_3$) δ14.5, CH_3; 61.2, CH_2; 122.2, C2'; 126.9, C2; 128.7, C5; 128.8, C3'; 129.1, C4; 130.2, C6; 131.2, C1; 131.8, C4'; 144.0, C3; 165.9, C=O; n.o. C1'.

(iv) 3-Phenyl-ONN-azoxybenzoic Acid

Ethyl 3-phenyl-ONN-azoxybenzoate (1.0 g) was hydrolysed with potassium hydroxide in ethanol to give

3-phenyl-ONN-azoxybenzoic acid (0.44 g), m.p. 195-197°(Found C, 64.6; H, 3.9; N, 11.6. $C_{13}H_{10}N_2O_3$ requires C, 64.5; H, 4.2; N, 11.6%). ν_{max} (Nujol) 1680 cm^{-1}, C=O.

3-Phenyl-NNO-azoxybenzoic Acid

(i) Ethyl 3-Phenyl-NNO-azoxybenzoate

Evaporation of the mother liquor from the crystallization of the -ONN- isomer gave a residue which was shown (^1H n.m.r.) to consist of a 5:1 mixture of the -NNO- and -ONN- isomers. This residue (0.42 g) was repeatedly adsorbed onto a silica/polyethylene glycol Chromatotron plate and eluted with light petroleum/ether mixtures finally giving pure ethyl 3-phenyl-NNO-azoxybenzoate (0.10 g), as a yellow oil. ν_{max} (liquid film) 1725 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 1.42, t, J7Hz, CH_3; 4.38, q, J7Hz, CH_2; 7.20-7.73, m, 5H, phenyl protons; 8.15-8.53, m, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.3, CH_3; 61.6, CH_2; 123.5, C2 ; 125.7, C2'; 126.4, C4 ; 128.8, C3'; 128.9, C5 ; 130.0, C4'; 131.6, C1 ; 132.4, C6 ; 144.8, C1'; 148.4, C3 ; 165.3, C=O.

(ii) 3-Phenyl-NNO-azoxybenzoic Acid

Ethyl 3-phenyl-NNO-azoxybenzoate (0.59 g) was hydrolysed with potassium hydroxide in ethanol to give 3-phenyl-NNO-azoxybenzoic acid (0.30 g), m.p. 181-182° (Found C, 64.6; H, 4.0; N, 11.5. $C_{13}H_{10}N_2O_3$ requires C, 64.5; H, 4.2; N, 11.6%). ν_{max} (Nujol) 1680 cm^{-1}, C=O.

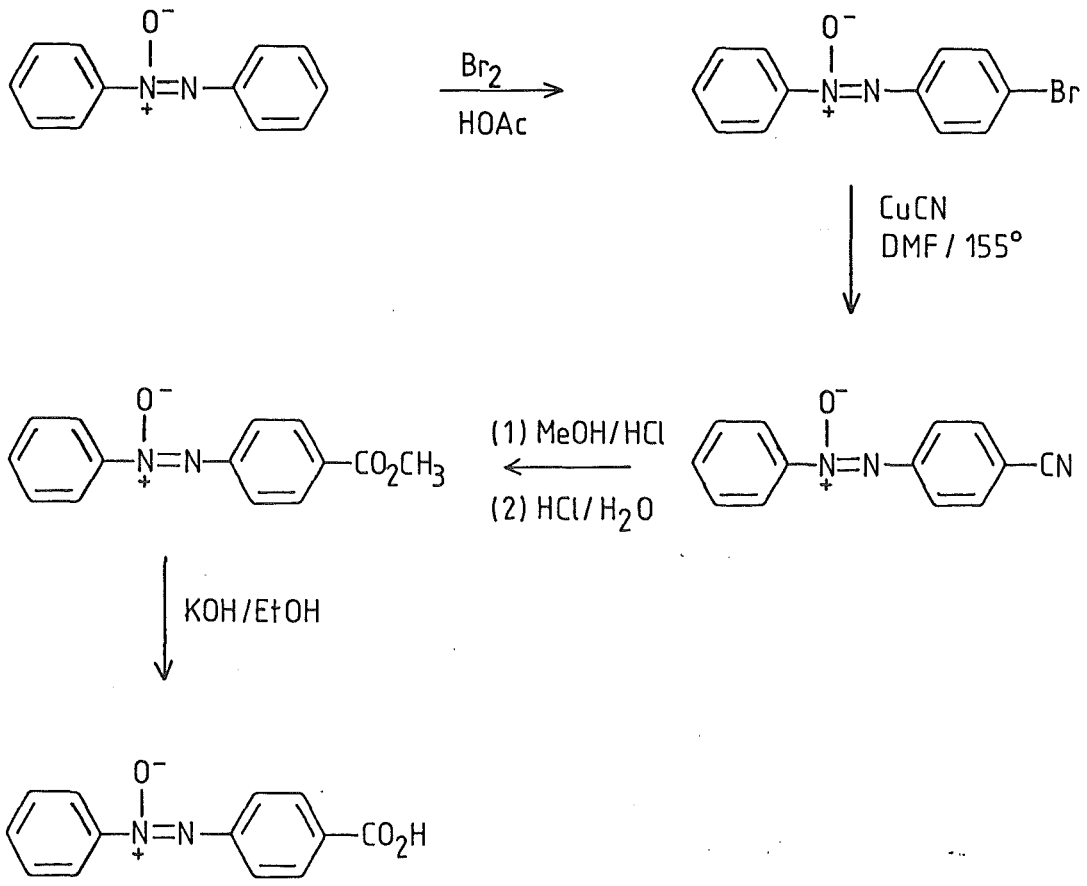
Preparation of 4-Phenyl-ONN- and 4-Phenyl-NNO-azoxybenzoic Acids

Attempts to separate the ethyl 4-phenylazoxybenzoate

isomers by fractional crystallization and chromatography failed.

4-Phenyl-ONN-azoxybenzoic Acid

The successful approach adopted was based on the readily available 4-bromo-ONN-azoxybenzene and functional group interconversion of the bromo substituent to the acid. The method is summarised below:



The preparation of the nitrile is an adaption of the method described by Friedman and Shechter.[69] The preparation of the ester, from the nitrile, is an example of the Pinner synthesis, which has been reviewed.[70]

saturated with anhydrous hydrogen chloride gas, stoppered, and left to stand in the dark for 24 h. Removal of the solvent under reduced pressure gave yellow crystals of the corresponding iminoester hydrochloride, m.p. 213-215°. ν_{max} (Nujol) 1640 cm^{-1}, C=N.

A solution of the hydrochloride in methanol (50 ml), water (50 ml) and concentrated hydrochloric acid (5 ml) was refluxed for 2 h. On chilling a yellow solid precipitated. This was filtered off and recrystallised from ethanol. It proved to be pure methyl 4-phenyl-ONN-azoxybenzoate (1.54 g), m.p. 138.5-140.5°. ν_{max} (Nujol) 1720 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 3.93, CH_3; 7.30-8.40, 9H, phenyl protons. ^{13}C n.m.r. δ 52.2, CH_3; 122.4, C2'; 125.1, C3; 128.9, C3'; 130.1, C2; 132.0, C4'; 147.3, C4; 166.3, C=O; n.o. C1', C1.

(iv) 4-Phenyl-ONN-azoxybenzoic Acid

Methyl-4-phenyl-ONN-azoxybenzoate (1.0 g) was hydrolysed with potassium hydroxide to give 4-phenyl-ONN-azoxybenzoic acid (0.56 g), m.p. 242-244° (lit. 231°[71]). (Found C, 64.6; H, 4.2; N, 11.8. $C_{13}H_{10}N_2O_3$ requires C, 64.5; H, 4.2; N, 11.6%). ν_{max} (Nujol) 1690 cm^{-1}, C=O.

4 -Phenyl-NNO-azoxybenzoic Acid

Fractional crystallization of a mixture of isomeric 4-bromoazoxybenzenes from ethanol gave the pure -NNO- isomer, which may be converted to the acid via the nitrile. The nitrile is hydrolysed directly to the acid in this case. Because the hydrolysis reaction conditions use hydrogen peroxide, a small sample of the acid was esterified and the esters carbon-13 n.m.r. spectra recorded to check that no

isomerization had occurred during the hydrolysis step. (The esterification reaction had been shown previously not to produce isomerization.)

The mixture of isomeric 4-bromoazoxybenzenes was prepared by the oxidation of 4-bromoazobenzene. This latter compound was obtained by the lithium aluminium hydride reduction of 4-bromo-ONN-azoxybenzene, which was in turn prepared by the bromination of azoxybenzene.

(i) 4-Bromoazobenzene

To a stirred solution of lithium aluminium hydride (0.71 g) in anhydrous ether (50 ml), a solution of 4-bromo-ONN-azoxybenzene (20 g) in anhydrous ether (120 ml) was added over 10 min. Afer an additional 15 min, water was cautiously added, the ether solution separated, dried with magnesium sulphate and the solvent removed under reduced pressure to give 4-bromoazobenzene (19 g), m.p. 86-88° (lit. 89°[72]).

(ii) 4-Bromoazoxybenzene

To a solution of 4-bromoazobenzene in acetic acid, 30% hydrogen peroxide was added in the normal manner to give a mixture of 4' and 4-bromoazoxybenzenes, m.p. 73-78°.

(iii) 4'-Bromo-NNO-azoxybenzene

Repeated fractional crystallization from ethanol of the isomeric 4-and 4'-bromoazoxybenzene mixture gave 4'-bromo-NNO-azoxybenzene, m.p. 94° (lit. 92°[73]). ^{13}C n.m.r. ($CDCl_3$) δ 123.8, C2'; 125.6, C2; 126.1, C4'; 128.7, C3; 129.8, C4; 131.8, C3'; 143.7, C1; n.o. C1'.

(iv) 4'-Cyano-NNO-azoxybenzene

4'-Bromo-NNO-azoxybenzene (1.54 g) was treated with

cuprous cyanide in DMF in a similar manner to that described earlier for the -ONN- isomer to give 4'-cyano-NNO-azoxybenzene (0.87 g), m.p. 120-122°. ν_{max} (Nujol) 2230 cm^{-1}, CN. ^{1}H n.m.r. ($CDCl_3$) δ 7.40-7.85, 5H, phenyl protons; 8.10-8.50, 4H, phenyl protons. ^{13}C n.m.r. δ115.2, C4'; 117.6, CN; 123.2, C2'; 125.9, C2 128.8, C3; 130.6, C4; 132.9, C3'; 143.5, C1; n.o. C1'.

(v) 4-Phenyl-NNO-azoxybenzoic acid

To a stirred solution of 4'-cyano-NNO-azoxybenzene (0.79 g) in ethanol (20 ml), a solution of 25% sodium hydroxide (0.1 ml) and 30% hydrogen peroxide (1 ml) was added. The solution was maintained at 45-50° for 2 h, then cooled and acidified with 5% sulphuric acid. The resulting precipitate was added to a solution of 25% sodium hydroxide (20 ml) in ethanol (50 ml) and refluxed for 90 min. The residue, after removal of the ethanol under reduced pressure, was acidified with 5% sulphuric acid and diluted with ether. The ether solution was dried with sodium sulphate and the solvent removed under reduced pressure. The yellow solid was recrystallised from ethanol to give 4 —phenyl-NNO-azoxybenzoic acid (0.55 g), m.p. 261-263° (lit. 241°[71]). (Found C, 64.4; H, 3.9; N, 11.5. $C_{13}H_{10}N_2O_3$ requires C, 64.5; H, 4.2; N, 11.6%). ν_{max} (Nujol) 1700 cm^{-1}, C=O.

Ethyl 3,5-Dimethyl-4-phenyl-ONN-azoxybenzoate

Oxidation of ethyl 3,5-dimethyl-4-phenylazobenzoate gave the corresponding azoxy derivative, the -ONN- isomer being the major product. (A similar result has been reported[74] for the oxidation of 2,6-dimethylazobenzene, where a 78:22 ratio of -ONN- to -NNO- isomers was observed). Separation of the

major -ONN- isomer was achieved by fractional crystallization of the crude product.

(i) Ethyl 3,5-Dimethyl-4-phenyl-ONN-azoxybenzoate

Ethyl 3,5-dimethyl-4-phenylazobenzoate (0.85 g) was oxidised in the normal way to give a yellow solid shown (^{1}H n.m.r., ^{13}C n.m.r.) to be a 4:1 mixture of the corresponding -ONN- and -NNO- isomers. Fractional crystallization from pentane gave ethyl 3,5-dimethyl-4-phenyl-ONN-azoxybenzoate (0.53 g), m.p. 79-80°. ν_{max} (Nujol) 1735 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.38, t, J7Hz, CH_3; 2.17, Me_2; 4.28, q, J7Hz, CH_2; 7.42-7.55, m, 3H, phenyl protons; 7.68, C2, C6; 8.17-8.38, m, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 14.4, CH_3; 17.5, Me_2; 60.9, CH_2; 122.5, C2'; 128.8, C1; 129.0, C3'; 129.4, C2; 130.3, C3; 132.4, C4'; 146.8, C4; 166.5, C=O; n.o., C1'.

(ii) 3,5-Dimethyl-4-phenyl-ONN-azoxybenzoate Acid

Ethyl 3,5-dimethyl-4-phenyl-ONN-azoxybenzoate (0.53 g) was hydrolysed with potassium hydroxide in ethanol to give 3,5-dimethyl-4-phenyl-ONN-azoxybenzoic acid (0.38 g), m.p. 253-255°. (Found C, 66.5; H, 5.2; N, 10.3. $C_{15}H_{14}N_2O_3$ requires C, 66.7; 5.2; N, 10.4%). ν_{max} (Nujol) 1690 cm^{-1}, C=O.

2.14 Preparation and Purification of the Benzoic and Phenylacetic Acid Standards

(i) Benzoic Acid Standards

Benzoic Acid

BDH Analar benzoic acid was used without further purification, m.p. 118-120° (lit. 122.1°[75]).

3-Chlorobenzoic Acid

A sample of 3-chlorobenzoic acid was available from within the department. It was purified on a silica Chromatotron plate as the ethyl ester, then hydrolysed with potassium hydroxide in ethanol, and recrystallized from ethanol, m.p. 147-148° (lit. 158°[75]).

3-Nitrobenzoic Acid

Fluka A.G. 3-nitrobenzoic acid was recrystallized from chloroform, m.p. 140-141° (lit. 140-142°[75]).

3,5-Dinitrobenzoic Acid

BDH 3,5-dinitrobenzoic acid was recrystallized twice from 50% aqueous ethanol, m.p. 197° (lit. 205°[75]).

(ii) Phenylacetic Acid Standards

Phenylacetic Acid

BDH phenylacetic acid was recrystallized from pentane, m.p. 75-77° (lit. 77°[75]).

3-Methylphenylacetic Acid

3-Methylbenzylmagnesium chloride, prepared from 3-methylbenzyl chloride (21 g) and magnesium turnings in anhydrous ether (80 ml), was decomposed with CO_2 according to the literature method.[76] The crude product was recrystallized from pentane to give 3-methylphenylacetic acid (9.5 g), m.p. 61° (lit. 62-64°[76]).

3-Bromophenylacetic Acid

3-Bromoacetophenone (10 g) was converted to the acid via

the Willgerodt-Kindler reaction by the method described in the literature.[77] Recrystallization from water gave 3-bromophenylacetic acid (0.45 g), m.p. 99°, (lit. 102-103°[77]).

3-Nitrophenylacetic Acid

3-Nitrobenzaldehyde (30.2 g) was converted to the acid via the Erlenmeyer azlactone synthesis by the method described in the literature.[78] Recrystallization from water gave 3-nitrophenylacetic acid (0.20 g), m.p. 112-114° (lit. 116-118°[78])

(iii) 3,5-Dimethyl-4-substitutedbenzoic Acid Standards

3,5-Dimethylbenzoic acid was prepared by the oxidation of mesitylene. The other 3,5-dimethyl-4-substituted benzoic acids, where the substituent are the methoxy, chloro and cyano groups, were prepared from ethyl 4-amino-3,5-dimethylbenzoate by diazonium salt reactions, followed by hydrolysis of the ester. The preparation of the chloro derivative is described in detail. A similar method was used for the methoxy and cyano derivatives.

3,5-Dimethybenzoic Acid

Mesitylene (25 g) was oxidised by refluxing in dilute nitric acid according to the literature method.[79] Recrystallization from ethanol gave 3,5-dimethylbenzoic acid (6.6 g), m.p. 163-166° (lit. 163.5-166.5°[79]). ν_{max} (Nujol) 1690 cm^{-1}, C=O.

4-Chloro-3,5-dimethylbenzoic Acid

Ethyl 4-amino-3,5-dimethylbenzoate (1.67 g) was dissolved in a solution of concentrated hydrochloric acid (2.2 ml) and

water (5 ml), then cooled to 0°. A cold solution of sodium nitrite (0.63 g) dissolved in water (5 ml) was added with stirring at 0-5°. A solution of cuprous chloride (1.09 g) in concentrated hydrochloric acid (4.5 ml) was then added and the mixture was heated at 60° until the evolution of gas ceased, (30 min). The mixture was cooled and extracted with dichloromethane. The dichloromethane extract was washed several times with water, dried over magnesium sulphate and the solvent removed under reduced pressure. The product was purified on a silica Chromatotron plate to give ethyl 4-chloro-3,5-dimethylbenzoate (1.34 g), m.p. 47-49°. ^{1}H n.m.r. (CCl_4) δ 1.37, t, J7Hz, CH_3; 2.42, Me_2; 4.30, q, J7Hz, CH_2; 7.62, H2, H6.

The ester was hydrolysed with potassium hydroxide in ethanol to give 4-chloro-3,5-dimethylbenzoic acid (0.88 g), m.p. 210-212° (lit. 217.5-218.5°[45]). ν_{max} (Nujol) 1700 cm^{-1}, C=O.

4-Cyano-3,5-dimethylbenzoic Acid

The diazonium salt prepared from ethyl 4-amino-3,5-dimethylbenzoate (2.0 g) was decomposed in a solution of cuprous cyanide (1.34 g) and potassium cyanide (1.96 g) in water (5 ml) to give the crude ester (1.35 g). The product was purified on a silica Chromatotron plate to give ethyl 4-cyano-3,5-dimethylbenzoate (1.19 g), m.p. 85.5-87°. ν_{max} (Nujol) 2220, CN; 1720 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 1.40, t, J7Hz, CH_3; 2.60, Me_2; 4.42, q, J7Hz, CH_2; 7.77, H2, H6.

The ester (1.19 g) was treated with potassium hydroxide in ethanol to give 4-cyano-3,5-dimethylbenzoic acid (0.83 g); m.p. 202-205° (lit. 216.5-218.5°[45]). ν_{max} (Nujol) 2240, CN,

1700 cm^{-1}, C=O.

3,5-Dimethyl-4-methoxybenzoic Acid

The diazonium salt prepared from ethyl 4-amino-3,5-dimethylbenzoate (1.96 g) was decomposed in a solution of concentrated sulphuric acid (5 ml) and water (10 ml), to give ethyl 3,5-dimethyl-4-hydroxybenzoate (1.84 g), m.p. 105-108° (lit. 113°[80]). ν_{max} (Nujol) 3400, OH; 1690 cm^{-1}, C=O. ^1H n.m.r. ($CDCl_3$) δ 1.37, t, J7Hz, CH_3; 2.26, Me_2; 4.30, q, J7Hz, CH_2; 7.65, H2, H6.

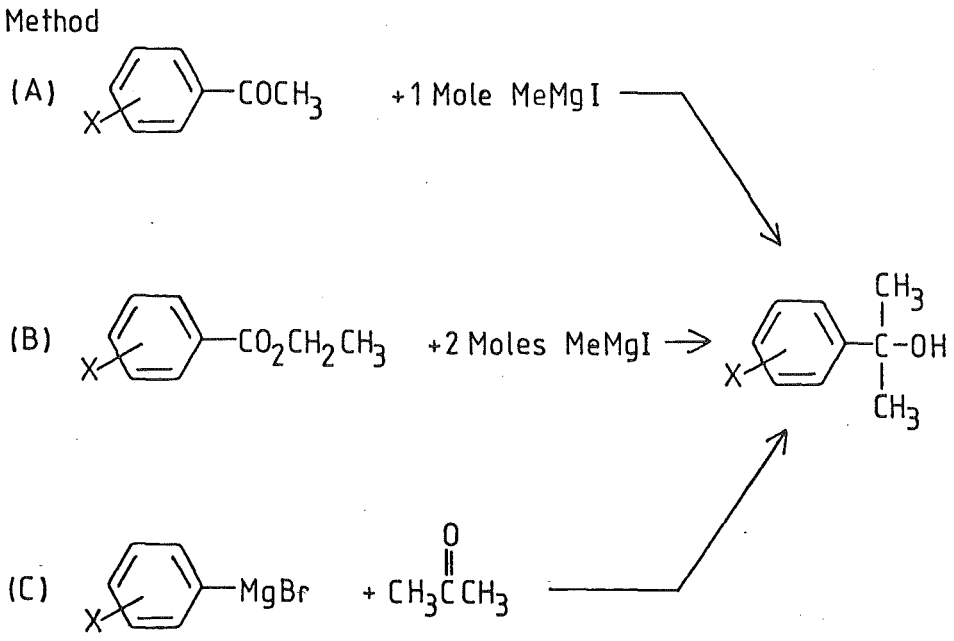
To a mixture of ethyl 3,5-dimethyl-4-hydroxybenzoate (1.84 g) and sodium hydroxide (0.54 g) in ethanol (10 ml) and water (10 ml) at 0°, dimethyl sulphate (1 ml) was added over 5 min. The mixture was stirred at room temperature for 30 min, then heated on a steam bath for 2 h. The mixture was cooled, diluted with ether, the solution washed with water, dried with magnesium sulphate and the solvent removed under reduced pressure. The residue was purified on a silica Chromatotron plate to give ethyl 3,5-dimethyl-4-methoxybenzoate (1.02 g), as an oil. ν_{max} (liquid film) 2950, CH; 1725 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 1.33, t, J7Hz, CH_3; 2.27, Me_2; 3.67, OMe; 4.17, q, J7Hz, CH_2; 7.52, H2, H6.

The ester (1.02 g) obtained was hydrolysed with potassium hydroxide in ethanol to give 3,5-dimethyl-4-methoxybenzoic acid (0.69 g), m.p. 180-182°. ν_{max} (Nujol) 1690 cm^{-1}, C=O.

2.2 Preparation of the Aryl dimethylcarbinols

Because of their sensitivity to moisture, the substituted phenyldimethylcarbinyl chlorides were prepared immediately before use from the corresponding phenyldimethylcarbinol. It was decided therefore to purify and characterize this product at the tertiary alcohol stage. (Other workers have also adopted this approach). The preparation of the chloride from the alcohol is described later in part 2.25.

The substituted phenyldimethylcarbinols were prepared via one of the Grignard reactions shown below:



2.21 Preparation of the Phenylazoaryldimethylcarbinols

These were usually prepared by the reaction of methyl-magnesium iodide with either the acetyl or carboethoxy

derivatives. Generally an excess of methylmagnesium iodide proved to be necessary to achieve good yields. The workup procedure is described in detail for 4-phenylazophenyldimethylcarbinol and was used throughout this thesis.

4-Phenylazophenyldimethylcarbinol

(i) 4-Phenylazoacetophenone

4-Aminoacetophenone (5 g) and nitrosobenzene (4 g) were condensed in the normal manner to give 4-phenylazoacetophenone (2.1 g), m.p. 108-110° (lit. 115°[80]). ν_{max} (Nujol) 1680 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 2.58, CH_3; 7.35-7.60, m, 3H, phenyl protons; 7.75-8.20, m, 6H, phenyl protons.

(ii) 4-Phenylazophenyldimethylcarbinol

Methylmagnesium iodide, (prepared from magnesium (0.13 g) and iodomethane in anhydrous ether (20 ml)), was added over 40 min to a solution of 4-phenylazoacetophenone (0.50 g in anhydrous ether (50 ml). The mixture was stirred for an additional 20 min before saturated aqueous ammonium chloride was added. The solution was washed with water, dried with magnesium sulphate and the solvent removed under reduced pressure. The residue was purified on a silica Chromatotron plate to give 4-phenylazophenyldimethylcarbinol (0.45 g), m.p. 90.5-91° (Found C, 75.2; H, 7.0; N, 11.7. $C_{15}H_{16}N_2O$ requires C, 75.0; H, 6.7; N, 11.7%). ν_{max} (Nujol) 3460 cm^{-1}, OH. ^1H n.m.r. (CCl_4) δ 1.56, Me_2; 1.95, OH; 7.32-8.33, m, 9H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 31.6, Me_2; 72.4, COH; 122.7, C3; 122.8, C2'; 125.2, C2; 129.0, C3'; 130.8, C4'; 151.3, C1; 152.2, C4; 152.6, C1'.

3,5-Dimethyl-4-phenylazophenyldimethylcarbinol

Ethyl 3,5-dimethyl-4-phenylazobenzoate (0.84 g), dissolved in anhydrous ether (70 ml), was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The dark red product was recrystallized from pentane to give 3,5-dimethyl-4-phenylazophenyldimethylcarbinol (0.45 g), m.p. 58-60° (Found C, 76.1; H, 7.5; N, 10.2. $C_{17}H_{20}N_2O$ requires C, 76.1; H, 7.5; N, 10.4%). ν_{max} (Nujol) 3350 cm^{-1}, OH. ^1H n.m.r. (CCl_4) δ 1.55, Me_2; 2.42, 3,5-diMe; 7.15, 2H, H2, H6; 7.37-7.53, m, 3H, phenyl protons; 7.70-7.97, m, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 19.2, 3,5-diMe; 31.7, Me_2; 72.4, COH; 122.5, C2'; 125.1, C2; 129.1, C3'; 130.7, C3; 130.9, C4'; 149.9, C1; n.o., C1', C4.

4-(2,6-Dimethylphenylazo)-3,5-dimethylphenyldimethylcarbinol

Condensation of 2,6-dimethylnitrosobenzene with a number of anilines failed to give any 2,6-dimethylazobenzenes. It is perhaps relevant to note that no condensations of this type have been reported in the literature.

A coupling of the diazonium salt prepared from ethyl 4-amino-3,5-dimethylbenzoate with 3,5-dimethylaniline, followed by deamination of the resulting ethyl 4-(4-amino-2,6-dimethylphenylazo)-3,5-dimethylbenzoate was attempted. (A similar approach was used successfully to prepare substituted 2,6-dimethylazobenzenes in Part II of this thesis). This method also failed, although coupling of the diazonium salt to 3,5-dimethylphenol did give ethyl 4-(4-hydroxy-2,6-dimethylphenylazo)-3,5-dimethylbenzoate, suggesting that steric factors were not hindering the condensation.

In the literature there are several methods reported for the oxidative coupling of anilines, usually by silver salts, to form symmetrical azobenzenes in moderate to low yields. The method we chose was that of cross-coupling of 2,6-dimethylaniline and ethyl 4-amino-3,5-dimethylbenzoate using silver carbonate supported on Celite catalyst. The preparation and applications of this reagent have recently been reviewed by McKillop and Young.[82] Small scale reactions involving refluxing the reactants and the oxidant in benzene indicated that the reaction proceeded slowly but cleanly, to give mainly the symmetrical 2,6,2',6'-tetramethylazobenzene, but with some ethyl 4-(2,6-dimethylphenylazo)-3,5-dimethylbenzoate. At 50°, the reaction did not proceed. The reaction conditions finally chosen were to reflux a four to one molar ratio of 2,6-dimethylaniline and ethyl 4-amino-3,5-dimethylbenzoate in toluene with 2 mole equivalents of silver carbonate supported on Celite. The reaction was monitored by proton-n.m.r.

(i) Ethyl 4-(2,6-Dimethylphenylazo)-3,5-dimethylbenzoate

A mixture of ethyl 4-amino-3,5-dimethylbenzoate (5.2 g), 2,6-dimethylaniline (13.1 g) and silver carbonate supported on Celite (2 mole equivalents) in toluene (400 ml), was refluxed for 13 h. The mixture was then filtered and washed with warm toluene (500 ml). The filtrate was evaporated to a small volume at reduced pressure and the dark red residue adsorbed onto a silica gel chromatographic column. Elution with light petroleum/benzene (1:1) gave 2,6,2',6'-tetramethylazobenzene (3.44 g), m.p. 44-48° (lit. 46-47°[74]). Elution with benzene gave a dark red solid that was further purified on a silica Chromatotron plate and recrystallized from light

petroleum/pentane (1:1) to give pure ethyl 4-(-2,6-dimethylphenylazo)-3,5-dimethylbenzoate (1.24 g), m.p. 60-62°. ν_{max} (Nujol) 1720 cm^{-1}, C=O. ^{1}H n.m.r. (CCl_4) δ 1.38, t, J7Hz, CH_3; 2.40, Me_2; 2.45, Me_2; 4.30, q, J7Hz, CH_2; 7.07, H3', H4', H5'; 7.75, H2, H6. ^{13}C n.m.r. ($CDCl_3$) δ 14.4, CH_3; 19.3, 2,6-diMe; 20.0, 3,5-diMe; 61.0, CH_2; 128.9, C1; 129.3, C4'; 129.4, C3; 129.6, C3'; 130.5, C2; 132.0, C2'; 150.8, C1'; 155.1, C4; 166.3, C=O.

(ii) 4-(2,6-Dimethylphenylazo)-3,5-dimethylphenyldimethylcarbinol

Ethyl 4-(2,6-dimethylphenylazo)-3,5-dimethylbenzoate (0.50 g) dissolved in anhydrous ether (15 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The red product was recrystallized from pentane to give 4-(2,6-dimethylphenylazo)-3,5-dimethylphenyldimethylcarbinol (0.44 g) m.p. 63.5-64.5° (Found C, 77.1, H, 8.5, N, 9.5. $C_{19}H_{24}N_2O$ requires C, 77.0, H, 8.2; N, 9.5%). ν_{max} (Nujol) 3250 cm^{-1}, OH. ^{1}H n.m.r. (CCl_4) δ 1.57, Me_2; 2.40, Me_2; 2.45, Me_2; 7.03, H3', H4', H5'; 7.13, H2, H6. ^{13}C n.m.r. ($CDCl_3$) δ 19.8, 2,6-diMe; 20.2, 3,5-diMe; 31.7, Me_2; 72.4, COH; 125.6, C2; 128.3, C4'; 129.4, C3'; 131.2, C3; 131.6, C2'; 149.4, C1'; 149.9, C1; 151.6, C4.

4-(2,6-Dimethylphenylazo)phenyldimethylcarbinol

Ethyl 4-(2,6-dimethylphenylazo)benzoate is prepared in Part II of this thesis, (by the condensation of ethyl 4-nitrosobenzoate with 2,6-dimethylaniline).

The purified alcohol was shown to be pure by carbon-13 n.m.r., but failed to give a satisfactory combustion analysis.

For this reason, the identity of the product was checked by high resolution mass spectrometry. In addition the 3,5-dinitrobenzoyl ester was prepared and analysed.

Ethyl 4-(2,6-dimethylphenylazo)benzoate (2.90 g) dissolved in anhydrous ether (50 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The product was distilled in a Kugelrohr apparatus at 185°/0.5 mm Hg to give 4-(2,6-dimethylphenylazo)phenyldimethylcarbinol (1.30 g) as a red oil. (Found $M^{+\cdot}$, 268.1581. $C_{17}H_{20}N_2O$ requires $M^{+\cdot}$ 268.1576). ν_{max} (liquid film) 3400, OH; 3000 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 1.55, Me_2; 2.33, 2 ,6 -diMe; 6.98, H3', H4', H5'; 7.47, 7.73, J_{AB} 9Hz, H2, H3, H5, H6. ^{13}C n.m.r. ($CDCl_3$) δ 18.7, 2 ,6 -diMe; 31.8, Me_2; 72.6, COH; 122.4, C3; 125.2, C2; 128.0, C4'; 129.1, C3'; 130.5, C2', 151.6, C1'; 152.3, C4; 163.8, C1. The 3,5-dinitrobenzoyl ester was prepared as an orange solid which was purified on a silica Chromatotron plate and recrystallized from carbon tetrachloride, m.p. 135° (Found C, 61.6; H, 4.7; N, 12.2. $C_{24}H_{22}N_4O_6$ requires C, 62.3; H, 4.8, N, 12.1%).

2.22 Preparation of the 4-Arylazophenyldimethylcarbinols

The 4-(X-substituted phenylazo)phenyldimethyl carbinols, (X= 4-methoxy, 4-methyl, 4-fluoro, 4-bromo and 3-bromo), were prepared from the corresponding ethyl 4-arylazobenzoate by the reaction with methylmagnesium iodide.

Because of the low solubility of these azo-esters in ether, freshly distilled THF was used as the reaction solvent. The Grignard reagent, however, was prepared in ether.

Purification of these dimethylcarbinols involved initial passage of the crude product through a short alumina chromatographic column. Elution with dichloromethane removed most impurities, allowing the alcohol to be eluted with methanol. This procedure is described in detail for the 4-methyl derivative and was used in all the other cases.

4-(4-Methylphenylazo)phenyldimethylcarbinol

(i) 4-Nitrosotoluene

4-Nitrotoluene (13.7 g) was reduced by the method of Barrow and Thorneycroft[83] to give a dark green oil that solidified on standing at 4°. It was shown (^{1}H n.m.r.) to consist of nearly pure 4-nitrosotoluene (6.7 g).

(ii) Ethyl 4-(4-Methylphenylazo)benzoate

4-Nitrosotoluene (4.7 g) and ethyl 4-aminobenzoate (6.4 g) were condensed in the normal manner to give orange crystals of 4-(4-methylphenylazo)benzoate (4.25 g), m.p. 101-102° (lit. 102.5-103.5°[84]). ^{1}H n.m.r. ($CDCl_3$) δ1.38, t, J7Hz, CH_3; 2.42, CH_3; 4.38, q, J7Hz, CH_2; 7.26, 7.83, J_{AB} 9Hz, 4H, phenyl protons; 7.87, 8.17, J_{AB} 9Hz, 4H, phenyl protons.

(iii) 4-(4-Methylphenylazo)phenyldimethylcarbinol

To a stirred solution of ethyl 4-(4-methylphenylazo)-benzoate (2 g) in freshly distilled THF (50 ml), an ethereal solution of methylmagnesium iodide (3 mole equivalents) was added over 30 min. The solution was refluxed for 30 min then cooled and neutralized with saturated aqueous ammonium chloride. The organic layer was dried with magnesium sulphate, the solvent removed under reduced pressure and the residue

adsorbed onto an alumina chromatographic column. After elution with dichloromethane, the alcohol was eluted with methanol then purified on a silica chromatotron plate. The orange crystals were recrystallized from light petroleum to give 4-(4-methylphenylazo)phenyldimethylcarbinol (0.98 g), m.p. 94-95° (Found C, 75.5; H, 7.2; N, 11.0. $C_{16}H_{18}N_2O$ requires C, 75.6; H, 7.1; N, 11.0%). ν_{max} (Nujol) 3350 cm^{-1}, OH; ^1H n.m.r. ($CDCl_3$)δ 1.62, Me_2; 1.87, OH; 2.42, CH_3; 7.25, 7.80, J_{AB} 9Hz, 4H, phenyl protons; 7.57, 7.85, J_{AB} 9Hz, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 21.4, CH_3; 31.7, Me_2; 72.6, COH; 122.6, C3; 122.8, C2'; 125.2, C2; 129.7, C3'; 141.4, C4'; 150.8, C4; 151.5, C1; 151.8, C1'.

4-(4-Methoxyphenylazo)phenyldimethylcarbinol

(i) Ethyl 4-(4-Methoxyphenylazo)benzoate

Ethyl 4-nitrosobenzoate (3.7 g) (see p.48) and 4-methoxyaniline (2.5 g) were condensed in the normal manner to give orange needles of ethyl 4-(4-methoxyphenylazo)benzoate (2.11 g), m.p. 93-95°. ^1H n.m.r. (CCl_4) δ1.40, t, J7Hz, CH_3; 3.83, OMe; 4.33, q, J7Hz, CH_2; 6.75-6.95, m, 2H, phenyl protons; 7.67-8.13, m, 6H, phenyl protons.

(ii) 4-(4-Methoxyphenylazo)phenyldimethylcarbinol

Ethyl 4-(4-methoxyphenylazo)benzoate (2.11 g) dissolved in freshly distilled THF (100 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The orange crystals were recrystallized from light petroleum to give 4-(4-methoxyphenylazo)phenyldimethylcarbinol (0.23 g), m.p. 104-105°. The purified alcohol failed to analyse correctly, although

shown to be pure by carbon-13 n.m.r. For this reason, the accurate mass of the alcohol and the analysis of the 3,5-dinitrobenzoyl ester were obtained. (Found $M^{+\cdot}$, 270.13680. $C_{16}H_{18}N_2O_2$ requires $M^{+\cdot}$, 270.13682). ν_{max} (Nujol) 3450 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.62, Me_2; 1.77, OH; 3.87, OMe; 6.90-7.05, m, 2H, phenyl protons; 7.50-8.00, m, 6H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 31.8, Me_2; 55.6, OMe; 72.5, COH; 114.2, C3'; 122.4, C3; 124.7, C2'; 125.2, C2; 147.1, C1'; 151.5, C1; 162.0, C4'; n.o. C4. The 3,5-dinitrobenzoyl ester was prepared as a yellow solid which was purified on a silica Chromatotron plate and recrystallized from dichloromethane-pentane, m.p. 108-110° (Found C, 58.5; H, 4.1; N, 12.0. $C_{23}H_{20}N_4O_7$ requires C, 59.5; H, 4.3; N, 12.1%).

4-(4-Fluorophenylazo)phenyldimethylcarbinol

(i) 4-Fluoronitrosobenzene

4-Fluoronitrobenzene (7.05 g) was reduced by the method of Mijs et al[85] to give a cream solid (5.2 g) which was shown (Infrared) to be a mixture of 4-fluoronitrosobenzene contaminated with some 4-fluoronitrobenzene. It was used without further purification.

(ii) Ethyl 4-(4-Fluorophenylazo)benzoate

The crude 4-fluoronitrosobenzene (5.2 g) and ethyl 4-aminobenzoate (6.0 g) were condensed in the normal manner to give orange crystals of ethyl 4-(4-fluorophenylazo)benzoate (1.19 g), m.p. 124°. ^1H n.m.r. ($CDCl_3$) δ 1.43, t, J7Hz, CH_3; 4.43, q, J7Hz, CH_2; 7.17-7.33, m, 2H, phenyl protons; 7.83-8.33, m, 6H, phenyl protons.

(iii) 4-(4-Fluorophenylazo)phenyldimethylcarbinol

Ethyl 4-(4-fluorophenylazo)benzoate (1.19 g) dissolved in freshly distilled THF (50 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner.

The light orange solid that was obtained was recrystallized from CCl_4 to give pure 4-(4-fluorophenylazo)phenyldimethylcarbinol (0.26 g), m.p. 103-104° (Found C, 69.6; H, 5.9; F, 7.3; N, 10.7. $C_{15}H_{15}FN_2O$ requires C, 69.8; H, 5.9; F, 7.4; N, 10.9%) ν_{max} (Nujol) 3400 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.60, Me_2; 1.90, OH; 6.97-8.00, m, 8H. ^{13}C n.m.r. ($CDCl_3$) δ 31.7, Me_2; 72.6, COH; 115.4/116.6, C3'; 122.7, C3; 124.6/125.0, C2'; 125.3, C2; 152.2, C4; n.o. C1', C4', C1.

4-(4-Bromophenylazo)phenyldimethylcarbinol

(i) 4-Bromonitrosobenzene

4-Bromonitrobenzene (10 g) was reduced to the nitroso derivative by the method described by Christoforou[50a] to give a light green solid (3.1 g).

(ii) Ethyl 4-(4-Bromophenylazo)benzoate

Crude 4-bromonitrosobenzene (3.1 g) and ethyl 4-aminobenzoate (3.0 g) were condensed in the normal manner to give orange crystals of ethyl 4-(4-bromophenylazo)-benzoate (1.31 g), m.p. 130°. ^1H n.m.r. ($CDCl_3$) δ1.40, t, J7Hz, CH_3; 4.35, q, J7Hz, CH_2; 7.47-8.23, m, 8H, phenyl protons.

(iii) 4-(4-Bromophenylazo)phenyldimethylcarbinol

Ethyl 4-(4-bromophenylazo)benzoate (1.31 g) dissolved in freshly distilled THF (100 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole

equivalents) in the normal manner. The orange solid was recrystallized from light petroleum to give pure 4-(4-bromophenylazo)phenyldimethylcarbinol (0.39 g), m.p. 113-114°. (Found C, 56.4; H, 4.7; Br, 25.5; N, 8.5. $C_{15}H_{15}BrN_2O$ requires C, 56.4; H, 4.7; Br, 25.0; N, 8.8%). ν_{max} (Nujol) 3350 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.65, Me_2; 1.78, OH; 7.50-7.97, m, 8H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 31.7, Me_2; 72.6, COH; 122.8, C3; 124.3, C2'; 125.3, C2; 132.3, C3; 151.3, C4; 151.4, C1'; 152.5, C1; n.o. C4'.

4-(3-Bromophenylazo)phenyldimethylcarbinol

(i) Ethyl 4-(3-Bromophenylazo)benzoate

Ethyl 4-nitrosobenzoate (5 g) and 3-bromoaniline (5 g) were condensed in the normal manner to give orange crystals of ethyl 4-(3-bromophenylazo)benzoate (3.75 g), m.p. 89°. ^1H n.m.r. ($CDCl_3$) δ 1.43, t, J7Hz, CH_3; 4.47, q, J7Hz, CH_2; 7.30-8.34, m, 8H, phenyl protons.

(ii) 4-(3-Bromophenylazo)phenyldimethylcarbinol

Ethyl 4-(3-bromophenylazo)benzoate (2 g) dissolved in freshly distilled THF (50 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The orange crystals were recrystalized from light petroleum to give 4-(3-bromophenylazo)-phenyldimethylcarbinol (0.12 g), m.p. 69-70°. (Found C, 56.7; H, 4.9; Br, 24.9; N, 8.8. $C_{15}H_{15}BrN_2O$ requires C, 56.4; H, 4.7; Br, 25.0; N, 8.8%). ν_{max} (Nujol) 3400 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.57, Me_2; 1.80, OH; 6.83-8.17, m, 8H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 31.8, Me_2; 72.6, COH; 122.9, C6'; 123.0, C3; 123.1, C3'; 124.6, C2'; 125.3, C2; 130.4,

C5'; 133.5, C4'; 152.2, C4; 152.8, C1; 153.6, C1'.

2.23 Preparation of the t-Butylazoaryldimethylcarbinols

4-t-Butylazophenyldimethylcarbinol

Ethyl 4-t-butylazobenzoate (1.5 g) (see page 49) dissolved in anhydrous ether (20 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The purified yellow product was recrystallized from pentane to give 4-t-butylazophenyldimethylcarbinol (1.0 g), m.p. 69.5°. (Found C, 70.6; H, 9.5; N, 12.6. $C_{13}H_{20}N_2O$ requires C, 70.9; H, 9.2; N, 12.7%). ν_{max} (Nujol 3300 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.35, Me_3; 1.57, Me_2; 2.30, OH; 7.53, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ27.0, Me_3; 31.8, Me_2; 67.5, $\underline{C}Me_3$; 72.5, COH; 121.7, C3; 125.0, C2; 151.0, C4; 151.1, C1.

4-t-Butylazo-3,5-dimethylphenyldimethylcarbinol

Ethyl 4-t-butylazo-3,5-dimethylbenzoate (0.76 g) dissolved in anhydrous ether (10 ml) was treated with an ethereal solution of methylmagnesium iodide (3 mole equivalents) in the normal manner. The yellow product was recrystallized from pentane to give 4-t-butylazo-3,5-dimethylphenyldimethylcarbinol (0.50 g), m.p. 58°. (Found C, 72.5; H, 9.8; N, 11.2. $C_{15}H_{24}N_2O$ requires C, 72.5; H, 9.7; 11.3%). ν_{max} (Nujol) 3500 cm^{-1}, OH. ^1H n.m.r. (CCl_4) δ 1.33, Me_3; 1.48, Me_2; 2.13, 3,5-diMe; 6.98, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ18.0, 3,5-diMe; 27.0, Me_3; 31.8, Me_2; 69.2, $\underline{C}Me_3$; 72.3, COH; 124.6, C2; 128.1, C3; 147.5, C1; 150.6, C4.

2.24 Preparation of the 4-Phenylazoxyaryldimethylcarbinols

Oxidation of 4-phenylazophenyldimethylcarbinol gave the corresponding azoxy compound, but attempts to separate the isomers failed.

The azoxy esters prepared earlier were found to react with the methyl Grignard reagent at the azoxy group to give unidentifiable products. However for reaction with 4-phenylazoxyacetophenone, the normal reaction with the acetyl group to give the tertiary alcohol was observed.

4 —Phenyl-NNO-azoxyphenyldimethylcarbinol

Fractional crystallization of 4-phenylazoxyacetophenone from methanol and benzene gave the -NNO- isomer, which was treated with a slight excess of methylmagnesium iodide to give the alcohol.

(i) 4-Phenylazoxyacetophenone

4-Phenylazoacetophenone (3 g) was oxidised in the normal manner with hydrogen peroxide in acetic acid to give an isomeric mixture of 4-phenylazoxyacetophenones (2.8 g).

(ii) 4 —Phenyl-NNO-azoxyacetophenone

Repeated fraction crystallizations of 4-phenylazoxyacetophenone initially from methanol and finally from benzene, gave yellow crystals of 4—phenyl-NNO-azoxyacetophenone, m.p. 135-136° (lit. 132° [81]). ν_{max} (Nujol) 1685 cm^{-1}, C=O. ^{1}H n.m.r. ($CDCl_3$) δ 3.45, CH_3; 7.20-7.60, m, 4H, phenyl protons; 7.90-8.40, m, 5H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 26.8, CH_3; 122.7, C3'; 125.8, C2; 128.8, C3; 128.9, C2; 130.2, C4; 139.2, C1'; 143.8, C1; 195.5, C=O, n.o. C4'.

(iii) 4-Phenyl-NNO-azoxyphenyldimethylcarbinol

4-Phenyl-NNO-azoxyacetophenone (1.0 g) dissolved in anhydrous ether (150 ml) was treated with an ethereal solution of methylmagnesium iodide (1.2 mole equivalents.) The yellow product obtained on work up slowly crystallized to give 4-phenyl-NNO-azoxyphenyldimethylcarbinol (0.94 g), m.p. 35-37°. ν_{max} (liquid film) 3450 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 1.63, Me_2; 1.92, OH; 7.30-7.70, m, 5H, phenyl protons; 8.07-8.40, m, 4H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 31.7, Me_2; 72.4, COH; 122.2, C3'; 125.0, C2'; 125.5, C2; 128.7, C3; 129.6, C4; 144.0, C1; 153.1, C4'; 172.7, C1'.

4-Phenyl-ONN-azoxyphenyldimethylcarbinol

(i) 4-Phenyl-ONN-azoxyacetophenone

The mother liquor obtained from the fractional crystallization of the -NNO- isomer was evaporated under reduced pressure to give a mixture of the -ONN- and -NNO- isomers in the ratio of 7:3 (^1H n.m.r.(benzene)). Attempted separation of the isomers in this mixture either on a silica Chromatotron plate or by fractional crystallization both failed. A tentative ^{13}C n.m.r. assignment for 4-phenyl-ONN-azoxyacetophenone was made on the basis of this mixture. ^{13}C n.m.r. ($CDCl_3$) δ 26.5, CH_3; 122.8, C2'; 125.3, C3; 128.9, C2, C3'; 132.1, C4'; 136.9, C1; 191.2, C=O; n.o. C4, C1'.

(ii) 4-Phenyl-ONN-azoxyphenyldimethylcarbinol

4-Phenylazoxyacetophenone (0.66 g) (7:3 mixture of -ONN- and -NNO- isomers) dissolved in anhydrous ether (100 ml), was treated with an ethereal solution of

methylmagnesium iodide (0.9 mole equivalents) in the normal manner to give the corresponding 4-phenylazoxyphenyldimethylcarbinols (0.24 g), shown (^{1}H n.m.r., ^{13}C n.m.r.) to be a 2:1 mixture of -ONN- and -NNO- isomers. (Found C, 70.3; H, 6.3; N, 10.7. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%). A tentative ^{13}C n.m.r. assignment for 4-phenyl-ONN-azoxyphenyldimethylcarbinol was made on the basis of the mixture. ^{13}C n.m.r. ($CDCl_3$) δ 31.6, Me_2; 72.5, COH; 122.3, C2'; 124.8, C2; 124.9, C3; 128.7, C3'; 131.5, C4'; n.o. C1, C4, C1'.

3,5-Dimethyl-4-phenyl-ONN-azoxyphenyldimethylcarbinol

3-Chloroperoxybenzoic acid (0.60 g) was added to a solution of 3,5-dimethyl-4-phenylazophenyldimethylcarbinol (0.59 g) in chloroform (20 ml) and the mixture left in the dark at 20° for 17 h. The solution was then washed with 3% aqueous sodium metabisulphate (20 ml), 10% sodium hydroxide (10 ml), water (20 ml), dried with magnesium sulphate and the solvent removed under reduced pressure. The yellow residue was shown (^{1}H n.m.r., ^{13}C n.m.r.) to be a 4:1 mixture of the -ONN- to -NNO- isomers. The mixture was adsorbed onto a silica Chromatotron plate. Elution with light petroleum/ether (10:2) gave a broad band, the initial part of which gave yellow crystals which were recrystallized from carbon tetrachloride and shown (^{13}C n.m.r.) to be the isomerically pure 3,5-dimethyl-4-phenyl-ONN-azoxyphenyldimethylcarbinol (0.18 g), m.p. 108-109°. (Found C, 71.5; H, 7.1; N, 9.8 . $C_{17}H_{20}N_2O_2$ requires C, 71.8; H, 7.1; N, 9.9%). ν_{max} (Nujol) 3450 cm^{-1}, OH. ^{1}H n.m.r. ($CDCl_3$) δ 1.60, Me_2; 1.77, OH; 2.17, 3,5-diMe; 7.22, H2, H6; 7.47-7.63, m, 3H, phenyl protons; 8.23-8.45, m, 2H, phenyl protons. ^{13}C n.m.r. ($CDCl_3$) δ 17.9, 3,5-diMe;

31.7, Me_2; 72.4, COH; 122.6, C2'; 124.3, C2; 128.9, C3'; 129.7, C3; 132.1, C4'; 141.4, C4; 147.7, Cl, n.o. Cl'.

2.25 Preparation of the Aryldimethylcarbinol Standards

The standard substituted phenyldimethylcarbinols were prepared by one of the methods shown on page 67. The method selected depended upon the availability of the starting materials. They were purified by distillation in a Kugelrohr apparatus under reduced pressure. The method of preparation, yields and physical properties of the standards are summarized in Table 6 .

2.26 Preparation of the Aryldimethylcarbinyl Chlorides

All the substituted phenyldimethylcarbinyl chlorides, except 4-phenyl-ONN-azoxyphenyldimethylcarbinyl chloride, were prepared by reacting the corresponding alcohol with an excess of thionyl chloride in the following manner.

General Method for the Preparation of the Aryldimethylcarbinyl Chlorides

To a stirred solution of the aryldimethylcarbinol (0.10 g) in anhydrous dichloromethane (5 ml), thionyl chloride (0.3 ml) was added and the solution stirred for 30 min. The solvent was removed under reduced pressure and the excess thionyl chloride removed under high vacuum. The purities of the product aryldimethylcarbinyl chlorides was checked by ^1H n.m.r., but their identity was not confirmed by microanalysis.

Table 6. Properties of the Aryldimethylcarbinol Standards

Substituent	Method	Yield(%)	mpt/bpt*	Lit mpt/bpt
H	A	72	90-103°/15mm	93°/11mm[86]
3-Methyl	C	44	90°/1mm	73°/3mm[86]
4-t-Butyl	B	33	77.5-79°	79°[86]
4-Fluoro	B	60	75°/1mm	86°/8.2mm[87]
4-Chloro †	A	70		
4-Bromo	A	40	102°/1mm ‡	45.6°[87]
3,5-Dimethyl	B	65	41-45°	

* The Kugelrohr oven temperature

† This compound was purified on the Chromatotron

‡ The oil slowly solidified on standing

4-Phenyl-ONN-azoxyphenyldimethylcarbinyl Chloride

The isomeric mixture of 4-phenylazoxyphenyldimethylcarbinols reacts with thionyl chloride to give an isomeric mixture of the corresponding chlorides. But hydrogen chloride gas reacts only with the -ONN- isomer. The -NNO- isomer remains as the carbinol.

A similar result was reported by Brown,[88] who found that 3-and 4-nitro-α-methylstyrene would not react with hydrogen chloride to form the dimethylcarbinyl chlorides.

The electronic nature of the -NNO- isomer is expected to be similar to that of a nitro group, so the lack of reactivity of the -NNO- isomer is not unexpected.

Anhydrous hydrogen chloride gas was bubbled through a solution of isomeric 4-phenylazoxyphenyldimethylcarbinols (0.15 g) in anhydrous ether (40 ml) for 1 h. The solvent was removed under reduced pressure and the excess hydrogen chloride was removed under high vacuum. The residue was shown (^{1}H n.m.r. and ^{13}C n.m.r.) to be a mixture of 4'-phenyl-NNO-azoxyphenyldimethylcarbinol and 4-phenyl-ONN-azoxyphenyl-dimethylcarbinyl chloride.

2.3 Measurement of pKa's

(i) Reagents

Ethanol

Ethanol (2l) was refluxed over calcium oxide (400 g) for 10 h, then distilled. It was then distilled from magnesium ethoxide and stored under nitrogen in tightly stoppered bottles.

Water

Double-deionized (Milli-Q) water was freed from CO_2 by boiling for 3 min, then cooling in an ice bath while nitrogen was bubbled through it.

0.2M Potassium Chloride

Dry potassium chloride (14.91 g) (Ajax, Analar) was dissolved in water (1L).

Potassium Hydroxide Solution 0.3-1.0M

Potassium hydroxide (8.4 g) (B.D.H., Analar) was washed briefly with water before being added to a 100 ml volumetric flask. The flask was made up to the mark with water. The base concentration was determined by titration against a known weight of potassium hydrogen phthalate dissolved in water.

Buffers

0.01M Borax and 0.05M potassium hydrogen phthalate buffers were prepared in 1L batches.

(ii) Measurement of pKa's

The pKa's were determined by a potentiometric titration of the substituted benzoic acid in 50% v/v 0.1M KCl-ethanol at 25°.

The pH was measured with a Beckman Research pH Meter using a Beckman E2 glass electrode (type 39004) and a Beckman calomel electrode (saturated with potassium chloride electrolyte). The electrodes were standardized against 0.05M potassium hydrogen phthalate and 0.01M borax buffers before and after each titration. A Gilmont glass syringe (2 ml) was used to deliver the standard potassium hydroxide solution.

The titration vessel consisted of a 100 ml jacketed flask with a glass top having glass joints allowing the placement of the electrodes, a nitrogen bubbler and the syringe needle into the flask. Water from a thermostatted water bath was circulated through the water jacket.

In a typical determination, 3.5×10^{-3} moles of the benzoic acid was placed in the titration vessel and ethanol (50 ml) was added. A clean teflon-coated magnetic follower was added and the mixture stirred. When the acid had dissolved, 0.2M potassium chloride solution (50 ml) was added. Ethanol is then added (the volume of one half the calculated volume of base required, typically 0.1-0.5 ml), and nitrogen (which has passed through a 50% v/v 0.1M KCl-ethanol solution at 25°C) was then bubbled through the solution for 20-30 min. The nitrogen flow was stopped and the solution titrated with the standardized potassium hydroxide solution, 10-20 pH/titre values being recorded in the buffer region. The titration was completed as quickly as possible

to minimise the effects of atmospheric carbon dioxide and electrode drift, the average run taking about half an hour. After each run the electrodes were soaked in distilled water for 30 minutes.

2.4 Calculation of pKa Values

For the equilibrium process

$$HA \quad H^+ + A^-$$

the dissociation constant Ka is given by

$$Ka = \frac{[H^+][A^-]}{[HA]} \quad \frac{\gamma H^+ \ \gamma A^-}{\gamma HA} \qquad (1)$$

From this equation the dissociation constant Ka can be calculated by measuring the pH of buffer solutions of the acid. This approach requires a knowledge of the magnitude of both the activity coefficients (γ) of the ions and the liquid junction potential, of the cell. In aqueous solvent, both of these factors have been shown to have a negligible effect on the pH. Thus the activity coefficients are assumed to be unity and the liquid junction potentials are of negligible magnitude. But in non-aqueous or mixed aqueous organic solvents, these two factors can not be ignored. Calculation of the magnitude of these effects is difficult, it being easier to measure their combined effect by calibrating the measured pH, pHm, to the actual hydrogen ion concentration, pHc, (the "calculated pH"), present in the solution.

The calibration method used was to add small amounts of dilute acid and base to a solution of 50% v/v 0.1M KCl-ethanol and measure the pHm. This is correlated with pHc to give a linear expression of the form

$$pHm = A\ pHc + B$$

where A and B are constants.

The pKa values were calculated in terms of the pHc values at each point in the buffer region using a computer. The calibration procedure and the computer program used will be discussed shortly. The average pKa value obtained from this program was finally expressed in terms of pHm, to give the apparent pKa of the acid in 50% v/v 0.1M KCl-ethanol at 25°.

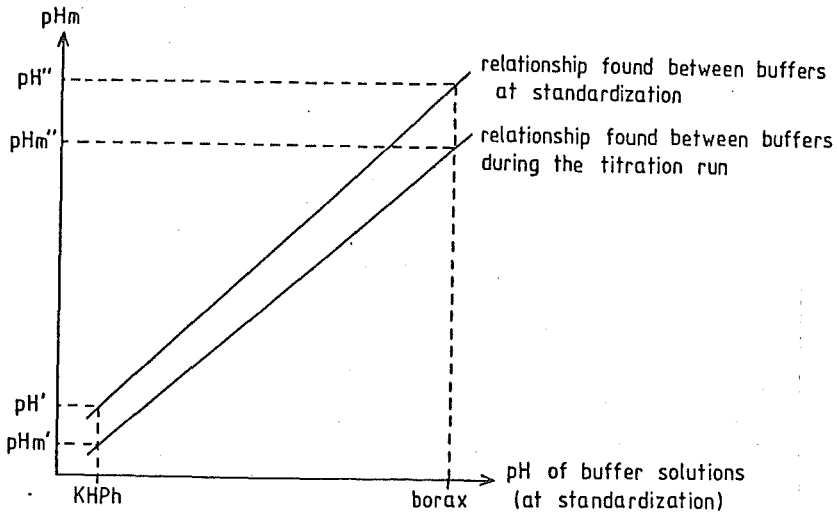
Before each titration run, the instrument was standardized to two buffer solutions.

(i) Buffer Correction to Individual pH Values

Measurement of the pH of the buffers before and after each titration run showed a small difference in pHm, to that observed during calibration. This difference was corrected for by the expression

$$pH = pHm \times SL - CORR$$

The SL and CORR terms are explained below:



pH' = pH of the KHPh at standardization, (instrument set to 4·008)

pH'' = pH of the borax at standardization

pHm' = the average of the two pHm(KHPh) values for the titration run

pHm'' = the average of the two pHm(borax) values for the titration run

KHPh = potassium hydrogen phthalate

$$SL = 1/\ \frac{pHm'' - pHm'}{pH' - pH'}$$

$$CORR = pHm' - pH'$$

Typically, values for SL were in the range 0.998 to 1.002, and for CORR, ± 0.005 to ± 0.050 were observed.

(ii) Calibration of pHm to pHc

In separate titrations, increments of dilute HCl and dilute KOH (up to 1 ml) were added to 100.05 ml of 50% v/v 0.1M KCl-ethanol under identical conditions to the experimental titration runs and the pHm recorded. The pHm was correlated with pHc, where pHc was calculated from the concentration of added acid or base. Least squares linear regression analysis gave the relationships between pHm and pHc. In this work two expressions between pHm and pHc were obtained (for work done at different times),

$$pHm = 1.0458\ pHc + 0.3189$$

$$pHm = 1.0032\ pHc + 0.4309$$

(iii) Calculation of pKa Values

Equation (1), remembering that the activity coefficient terms have been accounted for, was expanded in terms of

$[HA]_o$ = initial concentration of the acid at titre = 0

$[HA]_i$ = concentration of the acid at titre = i

$[H^+]_i$ = $[H^+]$ at titre = i

to give:

$$Ka = \frac{([HA]_o - [HA]_i + [H^+]_i).[H^+]_i}{[HA]_i - [H^+]_i} \qquad (2)$$

The pKa values were calculated, using this equation, by

a computer program. A copy of the program, together with a glossary of terms used is given on the following page.

```
C     CALCULATION OF PROTONATION CONSTANTS IN ETHANOL-WATER
      DIMENSION PH(20),V(20),AK(20),AAK(20),TITLE(18),W(20)
      READ(5,39) (TITLE(K),K=1,18)
      READ(5,40) TLI,VOL,ALK,CORR,SL,N
      READ(5,41) (W(I),PH(I),I=1,N)
      SIG=0.0
      DO 2 I=1,N
      V(I)=W(I)*1.00
      AH=SL*PH(I)-CORR
      AH=(AH-0.4309)/1.0032
      H=10.**(-AH)
      Q=VOL/(VOL+V(I))
      ATL=TLI*Q
      TH=ATL-ALK*V(I)/(VOL+V(I))
      AK(I)=(ATL-TH+H)*H/(TH-H)
      AAK(I)=-ALOG10(AK(I))
    2 SIG=SIG+AAK(I)
      AN=N
      AV=SIG/AN
      AAV=AV
      SIGD=0.0
      DO 3 I=1,N
    3 SIGD=SIGD+(AV-AAK(I))**2
      SD=SQRT(SIGD/(AN-1.0))
      WRITE(6,50) (TITLE(K), K=1,18)
      WRITE(6,52) (AAK(I),I=1,N)
      WRITE(6,53) AAV,SD
   39 FORMAT(18A4)
   40 FORMAT(E10.3,2X,4(F7.3,2X),I2)
   41 FORMAT(F6.3,2X,F6.3)
   50 FORMAT(//'CALCULATED VALUES OF LOG K FOR',18A4)
   52 FORMAT(10(F6.3,2X))
   53 FORMAT(/'AVERAGE PROTONATION CONSTANT',E10.5,2X,'STANDARD
     1DEVIATION',E10.3)
      CLOSE(5,STATUS='KEEP')
      CLOSE(6,STATUS='KEEP')
      STOP
      END
```

Glossary of Terms

AAK(I)	Calculated pKa value
AAV	AV
AK(I)	Calculated $[H^+]$ that corresponds to the calculated pKa
AH	pHm corrected for the buffer correction
ALK	Concentration of the standardized potassium hydroxide used
AN	N
ATL	$[HA]_o$, initial concentration of the acid at titre = o
AV	Average calculated pKa value
CORR	Buffer correction term
H	Calculated $[H^+]_i$
I	Counter for each point
N	Total number of pH/titre points used
PH(I)	pHm at titre = i
Q	Volume change factor after each addition of base
TH	$[HA]_i$
TITLE	Array to store the title of the experiment
TLI	$[HA]_o$, initial concentration of the acid at titre = O
SD	Calculated standard deviation of the pKa values
SIG	Sum of pKa values
SIGD	Sum of the difference between the average pKa and the individual pKa values
SL	Buffer correction term
V(I)	Titration volume values, or a constant value of them
VOL	Initial volume of the 50% 0.1M KCl/ethanol solution
W(I)	Titration volume values

2.5 Measurement of the Rates of Solvolysis

(i) Reagents

Acetone

Acetone (B.D.H., Analar) was used without further purification.

Water

Double-deionized (Milli-Q) water was used.

0.1M Sodium Hydroxide

Sodium hydroxide (0.40 g)(B.D.H., Analar) was dissolved in water (100 ml).

0.01M Borax

Sodium tetraborate (3.814 g)(B.D.H., Analar) was dissolved in distilled water (1L). Fresh solutions were prepared after 4 weeks.

Aqueous Acetone Solutions

As an example, 80% acetone-water solution is described. 200 ml of doubled-deionized water, (4 x 50 ml pipettes) was added to a 1L volumetric flask and made up to the mark with acetone with thorough mixing at room temperature. For each successive solution prepared, small amounts of acetone or water were added, if necessary, until a solvolysis rate identical (±2%) to that obtained with the original batch of solvent was observed.

(ii) Measurement of the Rates of Solvolysis of the Aryldimethylcarbinyl Chlorides

Brown and co-workers[86] measured the solvolysis rate by

preparing a solution of the aryldimethylcarbinyl chloride in 90% acetone-water at 25° and withdrawing aliquots at various times. The liberated hydrogen chloride was determined by titration of the aliquots with base. A different approach was followed by Fischer and co-workers in determining the σ_p^+ values of pyridine aza group by solvolysis of the pyridyldimethylcarbinyl chlorides.[89] Brown's method could not be used in this case because the acidic medium would lead to the unreactive pyridinium salt. To minimise this problem, they measured the solvolysis reaction rate with an automatic titrator at a constant pH of 8. We followed a similar approach to Fischer, choosing to monitor the reaction at pH 6.

In practice, rates only with half-lives in the range 3 to 30 minutes could be measured accurately. Because the compounds studied had reactivity extending outside this range, three solvent systems were used to cover this range, 87.5%, 80% and 72.5% acetone-water. Standard aryldimethylcarbinyl chlorides were measured in these solvents to define the ρ value.

The pH-Stat consisted of a Radiometer Automatic Titrator (Type TTTlc), a Radiometer Titrigraph (Type SBR2c) and a Radiometer Syringe Burette (Type SBUld).

The reactions were followed by using the pH-Stat to maintain the pH at 6 by the addition of dilute sodium hydroxide as the reaction (which liberated hydrochloric acid) proceeded. The phenyldimethylcarbinyl chloride (an amount calculated to require less than 1 ml of 0.1M NaOH), was added to the acetone-water solution (50-60 ml) in a jacketed cell containing both a glass and a calomel electrode, a

mechanical stirrer and the syringe needle. Water from a thermostatted water bath was circulated through the cell jacket. The solution was titrated with 0.1M sodium hydroxide, with a plot of volume of base used against time being recorded by the Titrigraph. Near the end of the reaction, the titration was completed manually to determine accurately the endpoint volume of base.

At the start of each day the electrodes were standardized to the borax buffer (pH 9.18 at 25.0°). Between each run, the electrodes were soaked in distilled water for 20-40 min.

The temperature of the water bath was maintained at 25.0°.

2.6 Calculation of the Rates of Solvolysis

The first order rate constants, k, were calculated from the slope of plots of log ($V_\infty - V_t$) versus t, where V_∞ is the total volume of base added (end point volume), and V_t is the volume of base added at time t.

These plots were linear over at least 70% of the reaction.

3. RESULTS

3.1 Calculation of pKa's

The results obtained from a typical run for 4-phenylazobenzoic acid are given below:

Concentration of 4-phenylazobenzoic acid = 8.21×10^{-4} M

Concentration of potassium hydroxide = 0.966 M

Calibration equation: pHm = 1.003pHc + 0.431

Buffer correction terms: SL = 1.001

CORR = 0.030

Titre (ml)	pHm	Calculated pKa
0.0200	4.696	4.579
0.0255	4.738	4.575
0.0250	4.780	4.572
0.0277	4.828	4.572
0.0300	4.865	4.567
0.0325	4.905	4.562
0.0350	4.947	4.560
0.0375	4.991	4.559
0.0400	5.029	4.551*
0.0425	5.078	4.555
0.0450	5.122	4.553
0.0475	5.170	4.553
0.0500	5.223	4.558

The average pKa value, in terms of pHc, excluding *, was found to be:

Average pKa = 4.565

Standard deviation = 0.008

The average pKa was expressed in terms of pHm by the calibration equation to give:

Average pKa for run = 5.009

The calculated pKa values obtained in this manner for the individual runs are listed in the following Tables, together with the average pKa value for each compound.

In all cases the solvent was 50% v/v 0.1M KCl-ethanol and the temperature was 25.0°.

Table 7. Calculated pKa Values for the Substituted Benzoic Acids

Substituent	Calculated pKa for Run No.					Average
	1	2	3	4	5	pKa
H	5.494	5.503	5.494	5.475	5.481	5.49
3-Cl	5.028	5.022	4.994			5.02
3-NO_2	4.435	4.436	4.446			4.44
3-Phenylazo	5.116	5.108				5.11
4-Phenylazo	5.009	5.023				5.02
3-t-Butylazo	5.185	5.164				5.17
4-t-Butylazo	5.108	5.103				5.11
3-Phenyl-ONN-azoxy	5.165	5.167				5.17
4-Phenyl-ONN-azoxy	5.100	5.137				5.12
3-Phenyl-NNO-azoxy	4.701	4.704				4.70
4-Phenyl-NNO-azoxy	4.794	4.782				4.79

Table 8. Calculated pKa Values for the Substituted Phenylacetic Acids

Substituent	Calculated pKa for Run No. 1	2	3	4	Average pKa
H	5.454	5.460	5.486	5.430	5.46
3-CH_3	5.554	5.538	5.510		5.53
3-Br	5.245	5.264	5.227		5.25
3-NO_2	4.938	4.952	4.934		4.94
4-Phenylazo	5.241	5.210	5.217		5.22

Table 9. Calculated pKa Values for the 4-Substituted-3,5-dimethylbenzoic Acids

Substituent	Calculated pKa for Run No. 1	2	3	Average pKa
H	5.688	5.674		5.68
OCH_3	5.714	5.700		5.71
Cl	5.354	5.348		5.35
CN	4.656	4.651		4.65
Phenylazo	5.434	5.445	5.427	5.44
t-Butylazo	5.480	5.490		5.49
Phenyl-ONN-azoxy	5.425	5.439		5.43

3.2 Calculation of the Rates of Solvolysis of the Aryldimethylcarbinyl Chlorides

The data obtained from a typical run for the solvolysis of 4-phenylazophenyldimethylcarbinyl chloride in 72.5% v/v acetone-water is given below:

V_∞ = 149

Time(min)	Vt	log(V_∞-Vt)
1	10	2.143
3	29	2.079
5	46	2.013
7	66	1.949
9	71	1.863
11	81	1.832
13	89	1.772
15	96	1.724
17	102	1.681

A plot of log (V_∞-Vt) against time gave a straight line with no noticeable curvature. A least squares linear regression gave the following parameters:

r^2 = 0.992

SD/RMS = 0.008

Slope = 0.0292 min^{-1}

From the slope the first order rate constant was calculated as:

k_1 = 11.2 x 10^{-4} sec^{-1}

The first order rate constants obtained in individual runs, together with the average rate constant, for each acetone-water system are given in the following Tables.

In all runs the temperature was 25.0°C,

Table 10. First Order Rate Constants for the Solvolysis of Substituted Phenyldimethylcarbinyl Chlorides in 87.5% v/v Acetone-Water at 25°

Substituent	$10^4 k_1 (sec^{-1})$ Individual Runs			Average
4-t-Butyl	39.4	39.2	45.1*	39.3
4-Fluoro	7.68	5.87*	7.45	7.57
3-Methyl	7.22	6.56	7.33	7.04
H	3.03	2.84		2.94
3,5-Dimethyl	10.2	10.4	10.4	10.3
3,5-Dimethyl-4-phenylazo	8.71	8.79		8.75
3,5-Dimethyl-4-t-butylazo	38.5*	33.6	34.1	33.9
3,5-Dimethyl-4-(2,6-dimethylphenylazo)	10.1	10.3	9.75	10.1
3,5-Dimethyl-4-phenyl-ONN-azoxy	20.7	20.3		20.5

* Omitted for averaging purposes

Table 11. First Order Rate Constants for the Solvolysis of Substituted Phenyldimethylcarbinyl Chlorides in 80% v/v Acetone-Water at 25°

Substituent	$10^4 k_1 (sec^{-1})$ Individual Runs				Average
H	20.1 20.2	20.3 20.7	21.0	21.7	20.8
4-Fluoro	40.3	56.6*	46.6	42.3	43.1
3-Methyl	37.3	38.5	39.2	45.6*	38.3
4-Chloro	6.06	6.60	7.52*		6.33
4-Bromo	5.03	5.07			5.05
4-Phenylazo	3.92	6.67*	4.11		4.02
4-(4-Methoxyphenylazo)	22.4*	15.9	16.0		16.0
4-Phenyl-ONN-azoxy	13.2*	12.2	12.0		12.1

* Omitted for averaging purposes

Table 12. First Order Rate Constants for the Solvolysis of Substituted Phenyldimethylcarbinyl Chlorides in 72.5% v/v Acetone-Water at 25°

Substituent	$10^4 k_1 (sec^{-1})$ Individual Runs			Average
4-Chloro	17.5*	19.9	19.1	19.5
4-Bromo	14.6	14.5	13.8	14.3
4-Phenylazo	11.3	11.2		11.3
4-t-Butylazo	14.8	14.6	13.5	14.3
4-(4-Methylphenylazo)	16.4	16.0	16.0	16.1
4-(4-Fluorophenylazo)	10.3	10.4	11.1	10.6
4-(4-Bromophenylazo)	8.06	7.91		7.99
4-(3-Bromophenylazo)	6.03	5.41	5.68	5.71

* Omitted for averaging purposes

4. DISCUSSION

4.1 Calculation of σ Values

4.11 Calculation of σ Values for the Unhindered Configuration

The normal σ values are calculated from the Hammett plots of the appropriate system. Thus the σ_m and σ_p values were found from the benzoic acid ionization data, the σ_p° value from the phenylacetic acid ionization data and the σ_p^+ values from the aryldimethylcarbinyl chloride solvolysis rate data.

(i) Calculation of the Unhindered σ_m, σ_p, σ° Values

The pKa values for the benzoic acid standards agree closely with those reported by Wepster.[90] These are shown in Table 13 below.

Table 13. pKa Values of the Substituted Benzoic Acids Used to Define the Reaction Constant

Substituent	Literature pKa	Measured pKa[A]
4-CH_3	5.69	
3-CH_3	5.60	
H	5.48	5.49
3-F	5.04	
3-Cl	5.01	5.02
3-Br	4.97	
3-NO_2	4.41	4.44
4-NO_2	4.29	
3,5-diNO_2[B]	3.41	3.42

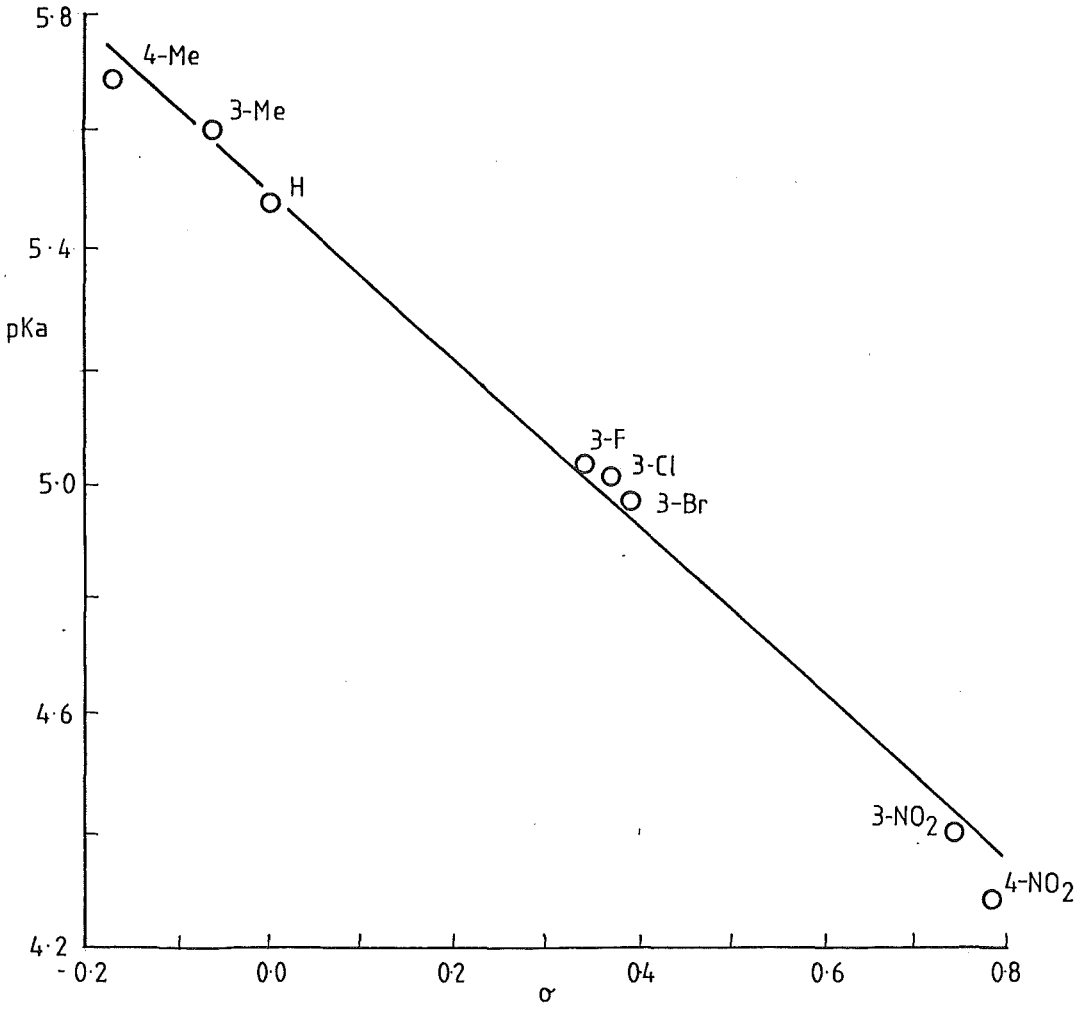
[A] This work

[B] This substituent was not used to define ρ, because of the uncertainty of its σ value.

The reaction constant, ρ, was calculated using both our values and those of Wepster, this being considered to give the most reliable ρ value.

The Hammett plot obtained using these substituents is shown in Fig. 1.

Fig 1 Hammett Plot for the pKa Values of the Substituted Benzoic Acids



The relevant parameters for the Hammett correlation are:

Reaction constant,	ρ	=	+1.46
Intercept,	pKa^H	=	5.49
Correlation coefficient,	r^2	=	0.993

These values for ρ and pKa^H were used to determine σ_m and σ_p values for the phenylazo, t-butylazo, phenyl-ONN-azoxy and phenyl-NNO-azoxy substituents. The results are given in Table 14.

Table 14. Values of σ_m, σ_p, for the Phenylazo, t-Butylazo, Phenyl-ONN-azoxy and the Phenyl-NNO-azoxy Substituents

Substituent	σ_m	σ_p
Phenylazo	+0.26	+0.33
t-Butylazo	+0.22	+0.26
Phenyl-ONN-azoxy	+0.22	+0.26
Phenyl-NNO-azoxy	+0.48	+0.55

The pKa values for the arylacetic acid standards, together with those reported by Wepster[91] are given in Table 15.

Table 15. pKa Values of the Arylacetic Acids Used to Define the Reaction Constant

Substituent	Measured pKa^A	Literature pKa
3-CH_3	5.53	5.56
H	5.46	5.47
3-Br	5.25	5.28
3-NO_2	4.94	4.98

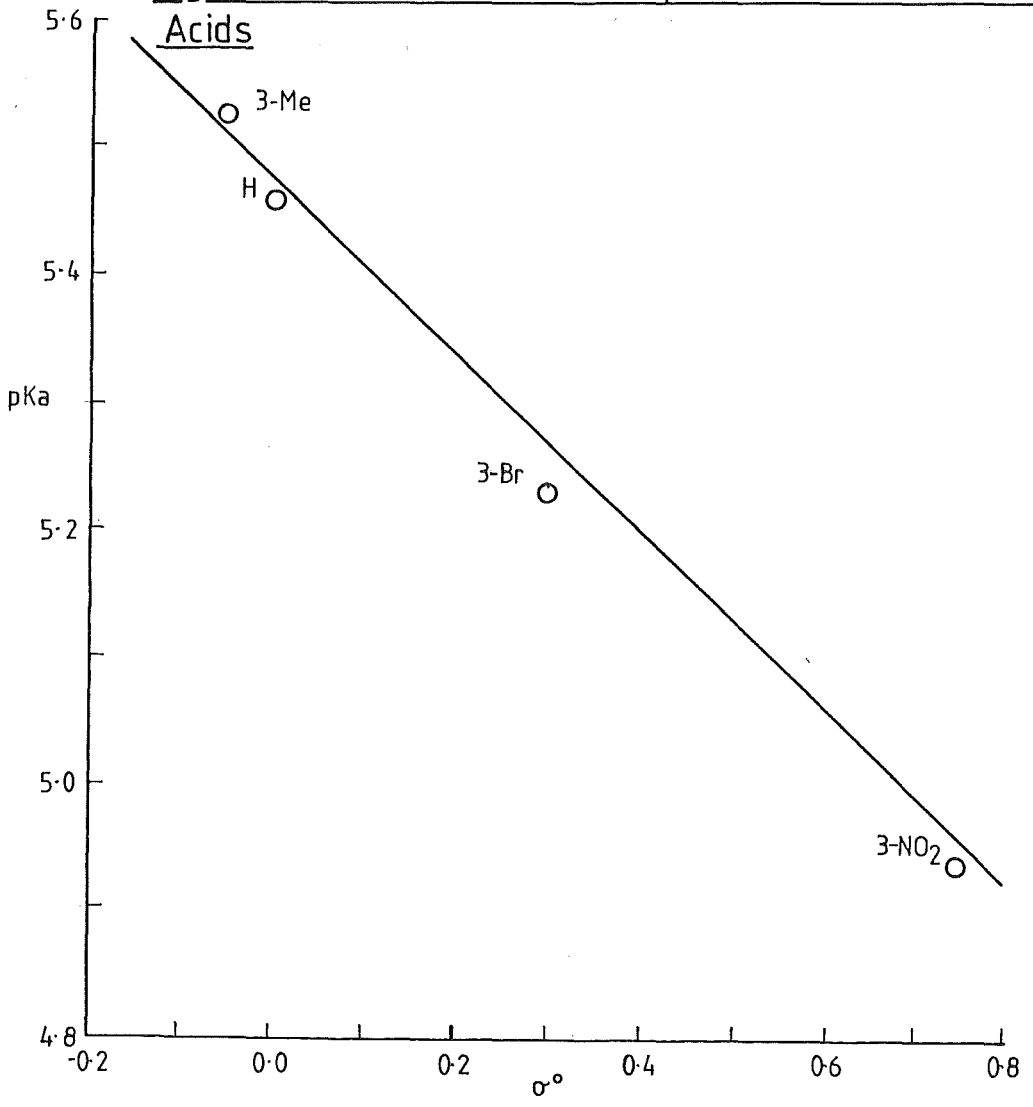
[A] This work

The reaction constant was calculated using the four standard arylacetic acids given in Table 15 giving a value of +0.701. The relevant parameters for the Hammett correlation are:

Reaction Constant	ρ	= +0.701
Intercept	pKa^H	= 5.48
Correlation Coefficient	r^2	= 0.990

The Hammett plot obtained using these substituents is shown in Fig. 2.

Fig 2 Hammett Plot for the pKa Values of the Arylacetic Acids



The ρ value is close to that reported by Wepster,[90] (+0.714). Using these parameters, a σ_p° value for the phenylazo substituent of +0.37 is obtained.

(ii) Calculation of the Unhindered σ_p^+ Values

Calculation of the reaction constant, ρ, for the solvolysis of the aryldimethylcarbinyl chlorides in 80% acetone-water using the data for phenyldimethylcarbinyl chloride, 4-fluoro, 3-methyl, 4-chloro and 4-bromophenyl-dimethylcarbinyl chlorides gave a value of -4.21. The relevant parameters for the Hammett correlation are:

Reaction constant	ρ	=	-4.21
Intercept	$\text{Log}k_1^H$	=	-2.69
Correlation coefficient	r^2	=	0.996

In the 72.5% acetone-water system, only two standards, the 4-chloro and the 4-bromophenyldimethylcarbinyl chlorides were measured. No reliable results could be obtained for the 3-chloro or the 3-bromophenyldimethylcarbinyl chlorides. It was therefore assumed instead that a ρ value similar to that found with the 80% acetone-water system, -4.21, and with the 87.5% acetone-water system, -4.24, (see page 113) applied also in 72.5% acetone-water. A value for ρ of -4.22 was chosen and was placed through a point midway between the 4-chloro and the 4-bromo standards. As it happened, most of the σ_p^+ values were relatively small, making them insensitive to changes in ρ.

The Hammett plots are shown in Figs. 3 and 4.

These parameters were used to calculate the σ_p^+ values for the unhindered phenylazo, 4-arylazo, 2,6-dimethyl-phenylazo, t-butylazo and phenyl-ONN-azoxy substituents. These values are listed in Table 16.

Fig 3 Hammett Plot for the Solvolysis of Aryldimethylcarbinyl Chlorides in 80% Acetone-Water at 25°

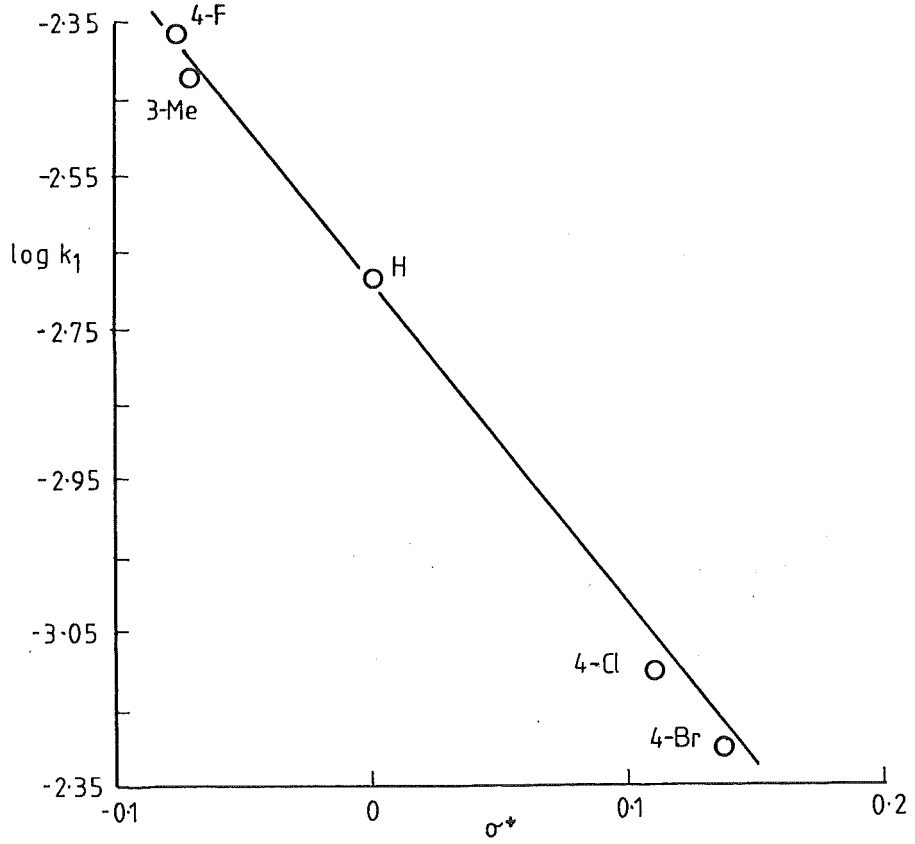


Fig 4 Hammett Plot for the Solvolysis of Aryldimethylcarbinyl Chlorides in 72·5% Acetone-Water at 25°

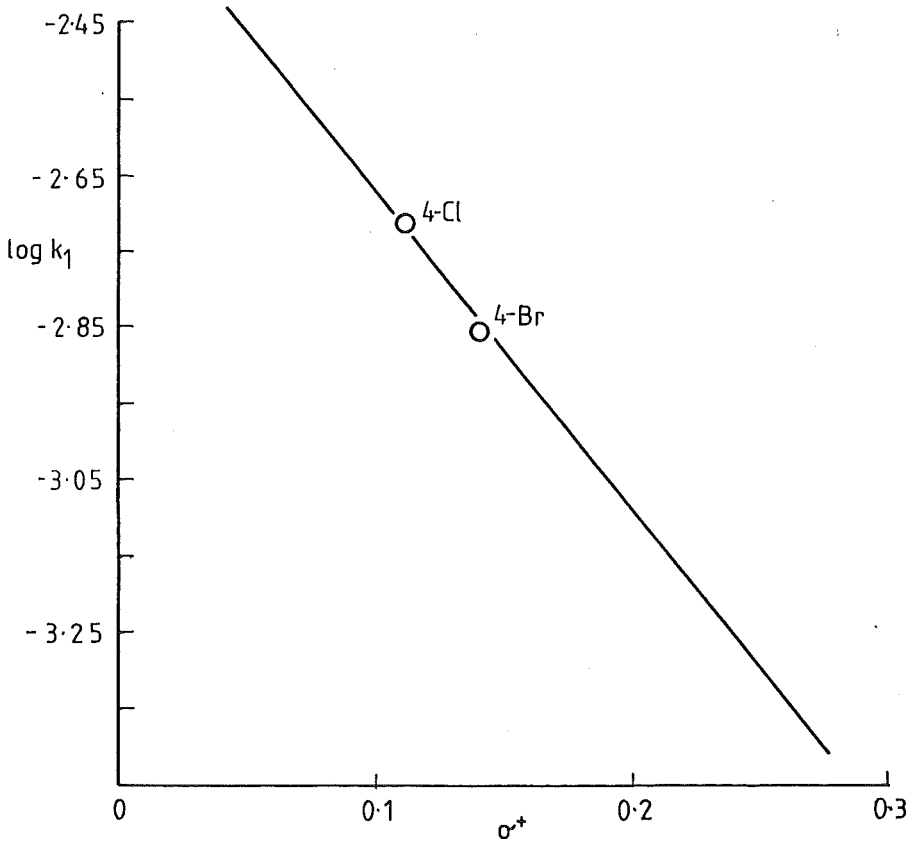


Table 16. Values of σ_p^+ for the Unhindered Phenylazo, 4-Arylazo, 2,6-Dimethylphenylazo, t-Butylazo and Phenyl-ONN-azoxy Substituents

Substituent	σ_p^+
Phenylazo	+0.17[A]
	+0.17[B]
4-Methoxyphenylazo	+0.03
4-Methylphenylazo	+0.13
4-Fluorophenylazo	+0.18
4-Bromophenylazo	+0.21
3-Bromophenylazo	+0.24
2,6-Dimethylphenylazo	+0.18
t-Butylazo	+0.15
Phenyl-ONN-azoxy	+0.06

[A] 80% Acetone-water solvent

[B] 72.5% Acetone-water solvent

(iii) Calculation of the Transmission Coefficient for the Unhindered *para* Azophenylene Linkage

The transmission coefficient, π', is given as:

$$\pi' = \frac{\rho(x\text{-}C_6H_4\text{-}N{=}N\text{-}C_6H_4\text{-}CMe_2Cl)}{\rho(X\text{-}C_6H_4\text{-}CMe_2Cl)}$$

where $\rho(X\text{-}C_6H_4\text{-}N{=}N\text{-}C_6H_4\text{-}CMe_2Cl)$ is the reaction constant obtained from a plot of the logarithm of the solvolysis rate for the *para*-arylazophenyldimethylcarbinyl chloride against $\sigma_p^+(X)$, and $\rho(X\text{-}C_6H_4\text{-}CMe_2Cl)$ is the reaction constant based on the solvolysis of the aryldimethylcarbinyl chloride

standards under identical conditions.

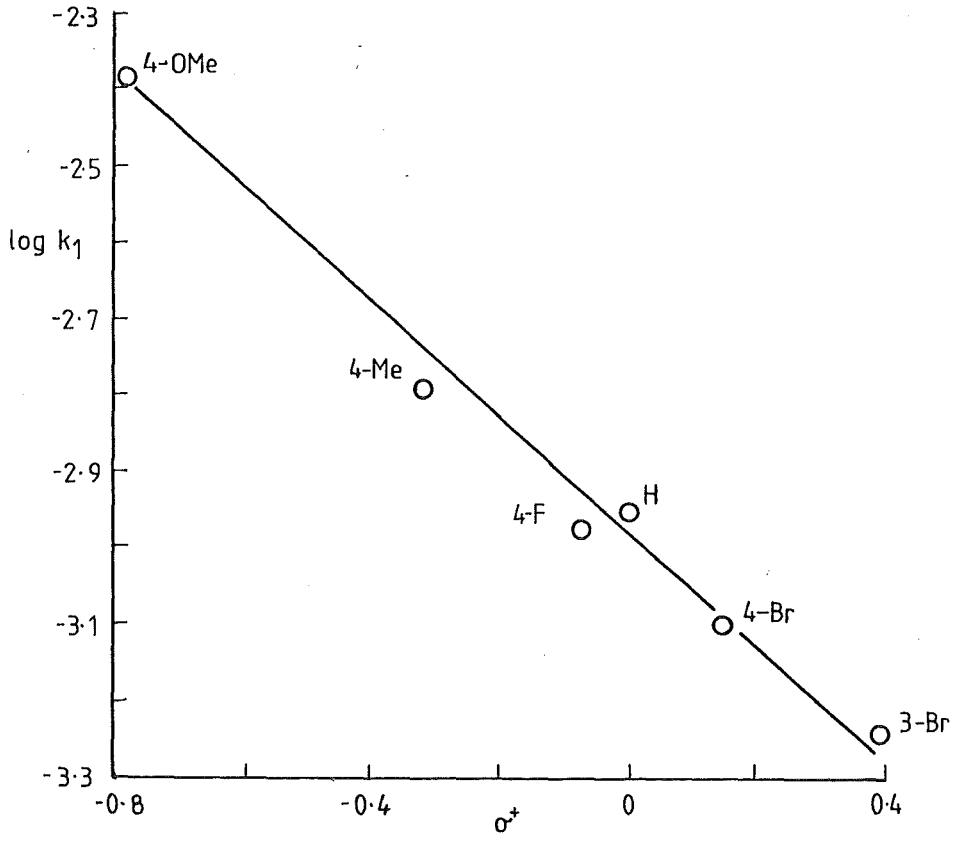
The solvolysis rates for all but the 4-methoxy substituted derivative were measured in 72.5% acetone-water. The solvolysis rate for the 4-methoxy substituted derivative in 72.5% acetone-water was calculated from its σ_p^+ value (obtained in 80% acetone-water).

A least squares linear regression on the $\log k_1$ values of all the *para*-arylazophenyldimethylcarbinyl chlorides (the substituents being 4-methoxy, 4-methyl, 4-fluoro, 4-bromo and 3-bromo), in 72.5% acetone gave a ρ value of -0.763. The relevant Hammett parameters are:

Reaction constant	ρ	=	-0.763
Intercept	$\log k_1^H$	=	-2.98
Correlation coefficient	r^2	=	0.983

The Hammett plot is shown in Fig. 5.

Fig 5 Hammett Plot for the Solvolysis of 4-Arylazophenyldimethylcarbinyl Chlorides in 72·5% Acetone-Water at 25°

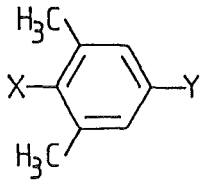


The ρ value is best defined by the *meta* substituents only, but in this case we have only one *meta* substituent, that being the 3-bromo derivative. A line through the hydrogen and 3 - bromo points yields a ρ value of -0.763, in excellent agreement to that found by using all the substituent points (although a different intercept value, i.e. $\log k_1^H$, is obtained).

The transmission coefficient is found to be 0.18, with an estimated error of ±0.03.

4.12 Calculation of σ Values for the Hindered Configuration

The "hindered" values are termed to be those where the substituent, X, is flanked by two methyl groups, as in



To measure the σ values in the hindered configuration, two approaches were used.

For the σ_p values, a Hammett correlation between the pKa's of the standard 4-X-3,5-dimethylbenzoic acids and $\sigma_p(X)$ was obtained. The σ_p value for the unknown substituent was found from the pKa of the corresponding 4-X-3,5-dimethylbenzoic acid using this Hammett plot.

For the σ_p^+ values, only the 3,5-dimethyl substituted standard was prepared. The assumption was made that a similar ρ value exists for the solvolysis of the 4-X-3,5-dimethylphenyldimethylcarbinyl chlorides to that measured for the 4-X-phenyldimethylcarbinyl chlorides. The hindered σ_p^+ values are determined by subtracting the σ_p^+ for the

3,5-dimethylaryl substituent from the σ_p^+ obtained for the 4-X-3,5-dimethylaryl substituent.

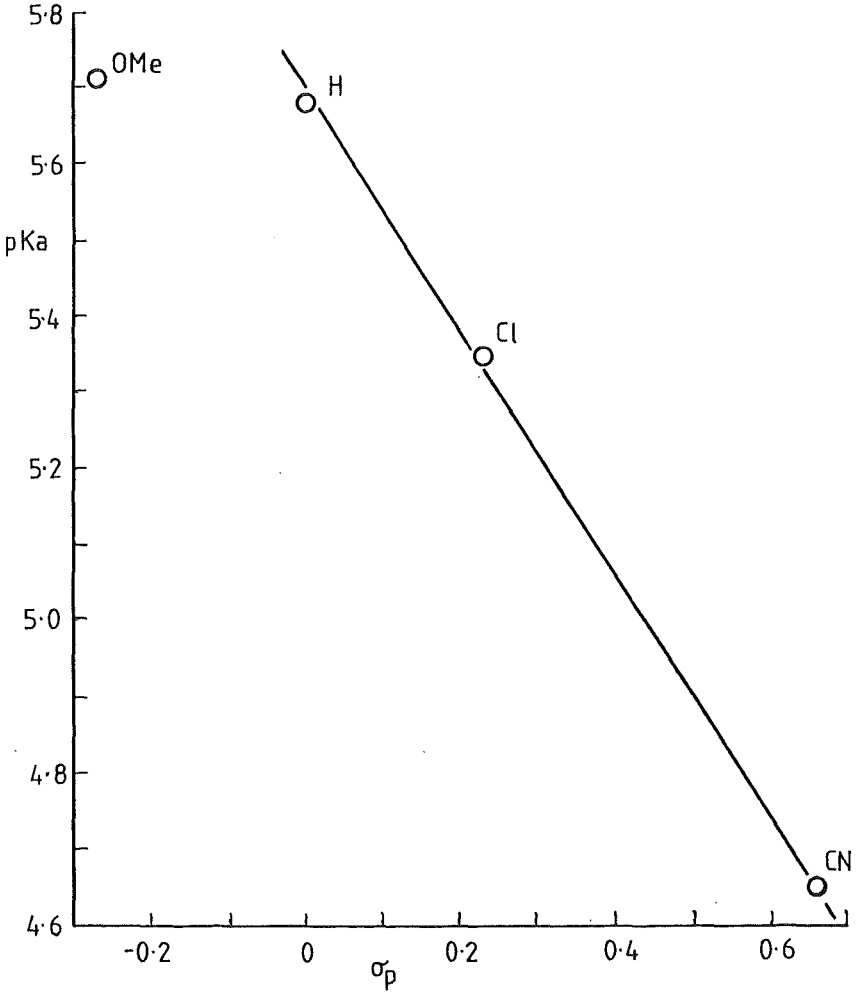
(i) Calculation of the Hindered σ_p Values

Calculation of the reaction constant, ρ, using the data for 3,5-dimethylbenzoic acid, 4-chloro and 4-cyano-3,5-dimethylbenzoic acid gave a figure of +1.59. The relevant parameters for the Hammett correlation are:

Reaction constant	ρ	=	+1.59
Intercept	pKa^H	=	5.69
Correlation coefficient	r^2	=	0.999

The Hammett plot is shown in Fig. 6.

Fig 6 Hammett Plot for the pKa Values of the 4-Substituted-3,5-dimethylbenzoic Acids



The pKa for 3,5-dimethyl-4-methoxybenzoic acid was measured but not used in calculating ρ; other workers had found this to be anomalous.[92] The ρ value obtained was used to determine the σ_p values for the hindered configurations of the phenylazo, t-butylazo and the phenyl-ONN-azoxy substituents. These results are shown in Table 17.

Table 17. Values of σ_p for the Hindered Phenylazo, t-Butylazo and the Phenyl-ONN-azoxy Substituents

Substituent	σ_p
Phenylazo	+0.16
t-Butylazo	+0.12
Phenyl-ONN-azoxy	+0.16

(ii) Calculation of the Hindered σ_p^+ Values

Calculation of the reaction constant, ρ, for the solvolysis of the aryldimethylcarbinyl chlorides in 87.5% acetone-water using the data for phenyldimethylcarbinyl chloride, 4-t-butyl, 4-fluoro and 3-methylphenyldimethyl-carbinyl chlorides gave a value of -4.24. The relevant parameters for the Hammett correlation are:

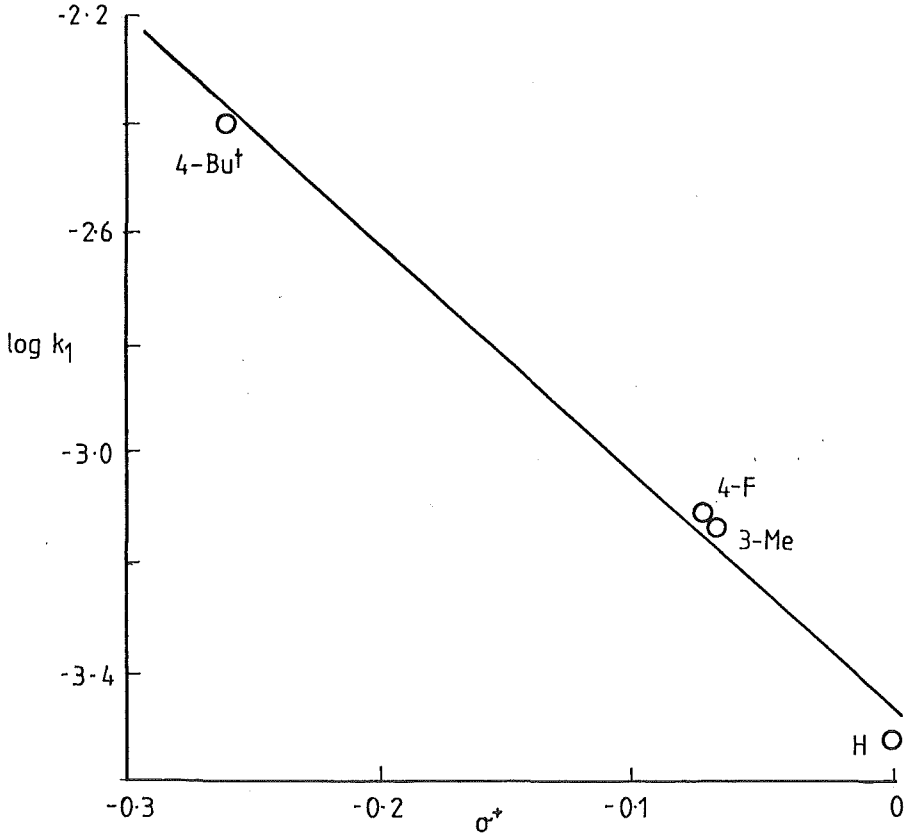
Reaction constant $\rho = -4.24$

Intercept $\log k_1^H = -3.47$

Correlation coefficient $r^2 = 0.989$

The Hammett plot is shown in Fig. 7.

Fig 7 Hammett Plot for the Solvolysis of Aryldimethylcarbinyl Chlorides in 87·5% Acetone-Water at 25°



These parameters were used to calculate the σ_p^+ values for the hindered phenylazo, t-butylazo, phenyl-ONN-azoxy and 2,6-dimethylphenylazo substituted 3,5-dimethyl groups. These values are given in Table 18.

Table 18. σ_p^+ Substituent Constants for the 4-Substituted 3,5-dimethyl Groups

Group	σp^+
3,5-dimethyl	-0.11
4-Phenylazo-3,5-dimethyl	-0.10
4-t-Butylazo-3,5-dimethyl	-0.24
4-(2,6-Dimethylphenylazo)-3,5-dimethyl	-0.11
4-Phenyl-ONN-azoxy-3,5-dimethyl	-0.19

The calculated hindered σ_p^+ values for the phenylazo, t-butylazo, phenyl-ONN-azoxy and the 2,6-dimethylphenylazo substituents are given in Table 19.

Table 19. σ_p^+ Values for the Hindered Phenylazo, t-Butylazo, 2,6-Dimethylphenylazo and the Phenyl-ONN-azoxy Substituents

Substituent	Hindered σ_p^+
Phenylazo	+0.01
t-Butylazo	-0.13
2,6-Dimethylphenylazo	0.00
Phenyl-ONN-azoxy	-0.08

4.13 Reliability of the Results

The reliability of the σ values obtained depended on two factors

(i) The accuracy with which the data could be measured, and

(ii) The sensitivity of the data to substituent effects.

The accuracy of the data was approximately constant for a given type of measurement. Thus the pKa's were reproducible to within ±0.02 units and the solvolysis rate constants to ±5%, although with very slow reactions the error may have been greater. Since the σ values were evaluated using the formula

$$\sigma x = \frac{\log k^X - \log k^H}{\rho}$$

the reliability of the σ values depends both on the reliability with which $\log k^X - \log k^H$ can be measured, and

on the reliability of the reaction constant, ρ. Of the two, the error in ρ is the more important since even if the value of $\log K^H - \log K^X$ is small, and the error is relatively large in percentage terms it becomes relatively small in absolute terms. But the errors in the ρ value can exert a considerable influence on the σ value, especially when the $\log k^X - \log k^H$ term is large and the ρ value relatively small.

It is generally accepted that carefully made measurements on systems such as the ionization of benzoic acids and the solvolysis of aryldimethylcarbinyl chlorides should lead to σ values with a reliability of no worse than ± 0.03 σ units. With our work, the majority of the σ values calculated are relatively low and the error could be less than this. But in the case of the phenylazo group, the σ_p° value is likely to be significantly less reliable than the groups σ_m or σ_p values because the ρ for this reaction (0.70) is much lower than that for the benzoic acid ionization reaction under the same conditions (1.46), while the precision of the measurement remains unchanged. An error of ± 0.03 to ± 0.05 in this case is considered likely.

The hindered σ_p^+ values were determined from the subtraction of two σ_p^+ values. The error with these values is therefore twice that of the unhindered σ_p^+ values.

4.14 Summary of the σ Values

A summary of all the unhindered and hindered substituent constants measured are given in Table 20.

Table 20. Summary of the Unhindered and Hindered Substituent Constants

Substituent		Unhindered			Hindered	
	σ_m	σ_p°	σ_p	σ_p^+	σ_p	σ_p^+
Phenylazo	+0.26	+0.37	+0.33	+0.17	+0.16	+0.01
4-Methoxyphenylazo				+0.03		
4-Methylphenylazo				+0.13		
4-Fluorophenylazo				+0.18		
4-Bromophenylazo				+0.21		
3-Bromophenylazo				+0.24		
2,6-Dimethylphenylazo				+0.18		0.00
t-Butylazo	+0.22		+0.26	+0.15	+0.12	-0.13
Phenyl-ONN-azoxy	+0.22		+0.26	+0.06	+0.16	-0.08
Phenyl-NNO-azoxy	+0.48		+0.55			

4.2 Discussion of the σ Values

In discussing the substituent constants determined for the various groups, we will first consider the groups in their normal or unhindered configuration, i.e. where no attempt has been made to prevent the molecule from achieving a coplanar structure in the transition state. We will then consider the change in the substituent constants that resulted when attempts were made at forcing a non-planar structure by hindering the coplanar one.

4.21 σ Values for the Unhindered Groups

4.211 The Phenylazo Group

For the phenylazo substituent, values for the σ_m and σ_p constants have been reported previously and were summarised in Tables 1 and 2 respectively on page 18. Our figure of +0.26 for σ_m compares well with the literature values, although it does appear to be a little lower than the value of +0.28 which the literature suggests is a reasonable figure. Our σ_p value of +0.33 is in slightly better agreement with the literature values than the σ_m value.

No value for σ_p^o has previously been reported in the literature and our value of +0.37 is only slightly higher than our σ_p value. With the reliability of the σ_p^o value not being as good as the σ_m and σ_p values we do not believe that this figure by itself is sufficiently higher than σ_p for us to conclude that there is any significant +R component in the σ_p value.

The σ_p^+ substituent constant for the phenylazo group has been estimated previously, based mostly on the rates of electrophilic aromatic substitution reactions. These

estimates were summarised in Table 4 on page 20. In contrast to σ_m and σ_p, the σ_p^+ value of +0.17 obtained in the current study based on the aryldimethylcarbinyl chloride solvolysis, differs substantially from the literature estimates. The problem in our case is that not only does the σ_p^+ value based on the solvolysis rate not agree with the electrophilic substitution rates, but the latter do not even agree with one another. Since Brown and Okamoto found that as far as they could ascertain, substituent constants calculated from this solvolysis reaction could be successfully correlated with the rates of electrophilic aromatic substitution, this would appear to confirm that there must be a special feature about the electrophilic substitution reaction in azobenzene. This may be either an abnormal substitution mechanism, or a different method of stabilization of the substitution transition state.

In all cases the electrophilic rates are higher than the solvolysis rate. While this could be due to an abnormal mechanism that enhances the substitution rate, it should be noted that a high σ_p^+ value was also obtained for the side-chain bromination of toluenes, a reaction that does not involve electrophilic substitution. The alternative is that the substitution mechanism is normal but the mechanism of stabilization of the transition state differs from reaction to reaction. For the phenylazo substituent this is a possibility because, as we have seen in the introduction, the phenylazo group is capable of stabilizing an electron deficient centre by using either its π system or the lone electron pair on the adjacent azo nitrogen.

Of all the literature σ_p^+ values, perhaps the most surprising is the observed difference between the chlorination reaction using chlorine acetate catalysed by perchloric acid[17] and of the bromination reaction with hypobromous acid catalysed by perchloric acid,[19] as these two reactions are superficially very similar. One important difference that exists between the two reactions is that the chlorination reaction uses appreciable quantities of silver ions as a chlorination catalyst. Complexes between azobenzene and silver salts have been reported in the literature and it is conceivable that under the chlorination reaction conditions complexation could occur. Even if the complexation reaction is reversible, the complex may exist long enough to give a species that is more susceptible to electrophilic attack than azobenzene. Miller observed that azobenzene reacted much faster than either benzene or azoxybenzene with chlorine acetate whereas the chlorination reaction with chlorine in acetic acid azobenzene reacted at a similar rate to benzene. Miller concluded that the chlorine acetate reaction was operating by a normal mechanism and that molecular chlorination was retarded by the coordination of chlorine molecules to the azobenzene molecule. In light of the high silver perchlorate concentration, we favour the opposite conclusion that the molecular chlorination reaction is the more reliable one with its slow reaction rate reflecting the high selectivity of the electrophilic species. We therefore treat the high reactivity, and high σ_p^+ value of the other with caution. (The other high value of -0.37 is also very unreliable as it

is based on an extrapolation using the Yukawa-Tsuno equation).[22] This therefore reduces the range of reliable σ_p^+ values for the phenylazo group to -0.187 to +0.17, still a 0.36 σ unit difference.

Our results for the phenylazo substituent confirm that while it is capable of behaving as a +R group, in most of its reactions it behaves as a -I -R group. Comparing our σ_m, σ_p values with the literature σ_p^- values shows that the -R effect is quite substantial, comparable in magnitude with the acetyl or nitro groups.

Substituent	σ_I	σ_m	σ_p	σ_p^-
Phenylazo		+0.26	+0.33	+0.68
Acetyl	+0.30	+0.38	+0.50	+0.71
Nitro	+0.67	+0.74	+0.77	+1.04

For the acetyl and nitro groups the resonance contribution to σ_m (i.e. $\sigma_m - \sigma_I$) is about +0.08 units. If the same is true for the phenylazo group, then a value for σ_I of 0.18-0.20, (depending upon the σ_m value selected) seems to be indicated. This compares well with the value reported by Taft and co-workers[31] of +0.19 based on ^{19}F n.m.r. chemical shifts of *meta*-substituted fluorobenzenes in non-polar solvents, but differs from that proposed by him for polar ones (+0.25).

The σ_I value and the σ_p^+ value obtained from the solvolysis studies are of similar magnitude. This, initially, would suggest that the solvolysis study may only have measured the σ_I value and that the σ_R^+ is negligible. A more likely alternative explanation, however, is that the true σ_R^+ is masked by the -R effect operating in the phenylazo-phenyldimethylcarbinyl chloride.

A better basis for estimating the true σ_R^+ value of the phenylazo group would seem to be to use the σ_p value as a base point rather than the σ_I value. This numerically gives a σ_R^+ value of about -0.16. Conceivably it could be slightly larger if there was a contribution to the +R effect in the σ_p value, i.e. if say $\sigma_p^o = 0.37$ as measured by us.

This interpretation, of course, requires that the azo group and the ring bearing the dimethylcarbinyl chloride group be coplanar, or at least approximately so, in the transition state, since the -R effect is only operating in the planar configuration. Loss of the -R effect would lead to a substantially more negative σ_p^+ value than that observed.

4.212 The Arylazo Group

The σ_p^+ values obtained from the solvolysis of the 4-arylazophenyldimethylcarbinyl chlorides are re-listed below for convenience.

Arylazo	H	4-OMe	4-Me	4-F	4-Br	3-Br
σ_p^+	+0.17	+0.03	+0.13	+0.18	+0.21	+0.24

There are a number of σ values reported for arylazo groups in the literature, but most are based on systems involving amines and phenols, systems in which the arylazo group will be behaving as a -I -R group. There are two instances, however, involving electron deficient reaction sites, where the arylazo group could be expected to behave as a +R group.

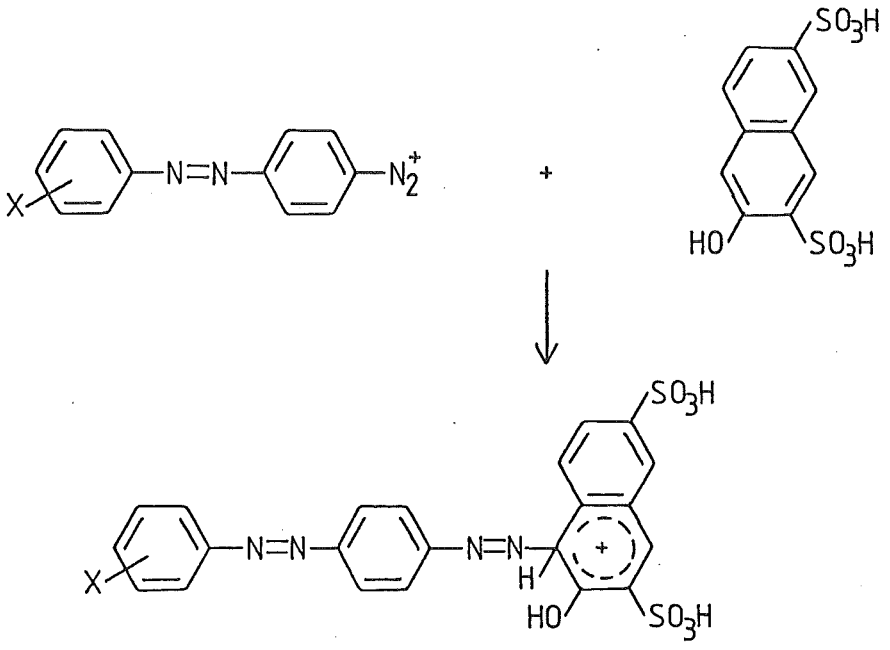
The most relevant is Christoforou's study of the bromination of azobenzenes[19] with $HOBr/H^+$, although only a

very limited range of compounds were studied, these are listed below:

Arylazo	H	3-Br	4-F
σ_p^+	+0.09	+0.20	+0.09

While his values are all less positive than the corresponding solvolysis values, similar trends are observed.

The other system where an electron deficient reaction site is present is the diazo-coupling reaction of 4-arylazodiazonium ions to R-acid, studied by Hashida and co-workers.[22] Here a transition state lying somewhere between a diazonium cation and an azo system is involved in the rate determining step.



The σ values obtained were

Arylazo	H	4-NMe_2	4-OH	4-Me	4-SO3H	4-NO_2
σ_p	+0.19	-0.10	+0.09	+0.16	+0.20	+0.28

These results are particularly interesting because although they have only 2 substituents in common (H and 4-Me) the numbers are very comparable to those obtained in our solvolysis reaction. This similarity between the two systems is even more interesting when one considers that Zollinger[93] had earlier found that this coupling reaction with substituted diazonium cations gave good correlations with ordinary Hammett σ_p values for substituents such as 4-OMe, 4-Me and 4-Br, and not the σ_p^+ values that are required for our solvolysis reaction. Fortunately, these results and the solvolysis results are not irreconcilable.

The diazonium cation is an extremely powerful -R group (σ_R ~ +1.5 to +2.0) and any arylazo group *para* to it would be expected to behave as a resonance donor (a +R group). However the transition state for the coupling reaction will be even more electron deficient. The σ constants determined therefore reflect changes in the resonance interaction between two highly electron deficient states. As Zollinger showed, the difference between the two is sufficiently small that they are adequately correlated by Hammett σ_p values rather than Brown's σ_p^+ values. Any contribution arising from the normal -R effect of the arylazo group to the energy of the ground and transition states will be present in both states. Therefore it will not appear in the difference between the two, of which the reaction rate may be regarded as a measure.

The solvolysis system, however differs from the diazo-coupling reaction in that the ground state is not electron deficient, but the transition state is. Therefore in

progressing from the -R ground state to the +R transition state, the energy needed to overcome the -R effect to produce a "+R transition state" is an extra factor that was not present in the diazo-coupling reaction. Since the solvolysis system normally gives good correlations with σ_p^+, then most substituents contribute stabilization equivalent to σ_R^+ to the transition state. This is also the case for arylazo groups, but because much of this is taken up in overcoming the contribution from the -R effect, the actual effect on the rate is smaller than one would have expected.

4.213 Transmission of Electronic Effects through the Azo Linkage

From the solvolysis data the efficiency with which substituent effects are relayed through the azophenylene linkage can be investigated.

For inductive effects the best guide is that provided by the *meta*-substituents. The data for the H and *meta*-bromo derivatives yield a π_p' value of 0.18. Using the same two points for Christoforou's bromination data, a value of 0.29 for π_p' is obtained, one which is 50% higher than that of the solvolysis data. On the assumption that the main mode of transmission of inductive effects is via the field effect of the substituent, and that the strength with which this is experienced is inversely proportional to the square of the distance, then the relative values of π_p' for the two systems are consistent with the site of developing charge (which is not necessarily the same as the reaction site) in our solvolysis system being closer to the substituent than in the electrophilic aromatic substitution. Such a situation seems highly improbable; the reverse would in fact be

predicted. There is also some evidence that π_p' for nucleophilic aromatic substitution is higher than that observed for the ionization of 4-arylazophenols.[94a] This is in agreement with the bromination and solvolysis results, but again in conflict with what we would expect.

There are also problems in explaining the observed efficiencies of transmission of resonance effects. The observations can be put on a quantitative basis by separating the observed σ constants for the *para*-derivatives into their inductive and resonance components. If one assumes that $\rho_I^{meta} = \rho_I^{para}$ then the contribution of the inductive effect of the substituent can be calculated and the σ_R component obtained by difference. Calculations on this basis show that the rate-accelerating effect of the 4-methoxy group is about twice that observed for the 4-fluoro group, four times that of 4-bromo and five times that of 4-methyl. These ratios are not consistent with interactions of either the σ_R^{o}, σ_R^{BA} or σ_R^{+} type, or indeed any intermediate type between these scales. The difficulty appears to lie with the 4-methoxy value, the strongest +R substituent. The results are most consistent with $\rho_I \sim \rho_R$, interactions of the σ_R^{BA} type (or thereabouts) for 4-bromo, 4-methyl and 4-fluoro, and of the type σ_R^{+} for 4-methoxy. There is no obvious explanation for the results although it would instinctively appear possible that over extended distances the attenuation of resonance effects for strong +R groups may be less than that for weaker +R groups. There are in fact some signs that this may be the case for ^{13}C n.m.r. chemical shifts.

4.214 The 2,6-Dimethylphenylazo Group

The σ_p^+ value for the 2,6-dimethylphenylazo group based on the aryldimethylcarbinyl chloride reaction is +0.18. As we noted in the Introduction, the presence of the two methyl groups in the non-reacting ring should reduce the overlap between the π orbitals of the phenyl group and the π orbitals of the azo system. This would have the effect of reducing the +R effect of the 2,6-dimethylphenyl group, if not eliminating it altogether, (although this may be partly offset by the +I effect of the methyl groups). Our results obtained in the previous section showed that the effect of introducing one methyl group at the *para* position of a phenylazo group is to decrease the σ_p^+ value by 0.04 units. The effect of two *ortho* methyl groups might reasonably be expected to be about twice that, i.e. about -0.08 units. Therefore if coplanarity were not inhibited by these groups, the σ_p^+ value for the 2,6-dimethylphenylazo group should be about +0.09. The actual value measured of +0.18 is virtually identical to that of the phenylazo group.

Total loss of coplanarity between the phenyl group and the azo linkage would be expected to give a σ_p^+ value more positive than that of a planar phenylazo group. That the observed σ_p^+ value for the 2,6-dimethylphenylazo group is not significantly greater than the phenylazo case may indicate that either coplanarity is not entirely lost in this system or else that the inductive effect of the introduced methyl substituents exactly counterbalances the loss of coplanarity almost exactly. Which of these two is the case is difficult to decide. However, if our belief that a planar

intermediate is involved in the solvolysis reaction is correct, then the first explanation of the two is the more likely to be correct.

4.215 The t-Butylazo Group

No Hammett σ values for either this or any other simple alkylazo substituent have been previously reported. The values obtained in our investigation are listed below, along with the corresponding σ values for the phenylazo group for comparison purposes.

	σ_m	σ_p	σ_p^+
t-butylazo	+0.22	+0.26	+0.15
phenylazo	+0.26	+0.33	+0.17

The two substituents parallel each other very closely showing that the t-butylazo group, like the phenylazo group, is likely to be a -I -R substituent under most conditions, but capable of exerting a +R effect under suitable circumstances. The σ_m and σ_p values are consistent with a σ_I for the t-butylazo group of around +0.15, somewhat less than what we estimated for the phenylazo group (about +0.18). Since the phenyl group is a -I one (σ_I = +0.10) whereas the t-butyl group is +I (σ_I = -0.07), then a σ_I value for the t-butylazo group less than that for phenylazo is expected, although the actual magnitude of the difference (0.03 units) appears to be somewhat less than we might have anticipated.

The σ_p^+ value recorded for the t-butylazo group is less than that recorded for the phenylazo group by about the same amount as the difference between the σ_I values. However this does not imply that the σ_R^+ values for the two groups are the

same. Applying the same reasoning as in the phenylazo case and comparing the difference between σ_p and σ_p^+ values, we arrive at a σ_R^+ value of -0.11. This compares with a σ_R^+ value for the phenylazo group of -0.16. This implies that in the planar azo system, the phenylazo group is a significantly stronger resonance donor than the t-butylazo group. This is not surprising as the phenyl group is a stronger resonance donor ($\sigma_R^+ = -0.27$) than the t-butyl group ($\sigma_R^+ = -0.17$). Since the non-reacting phenyl group can only exert a +R effect if it is coplanar with the azo group, then this result may be regarded as supporting evidence for a fully coplanar azobenzene system in our solvolysis reaction.

4.216 The Phenyl-ONN-azoxy and Phenyl-NNO-azoxy Groups

The substituent constants measured in our study are listed below:

	σ_m	σ_p	σ_p^+
Phenyl-ONN-azoxy	+0.22	+0.26	+0.06
Phenyl-NNO-azoxy	+0.48	+0.55	

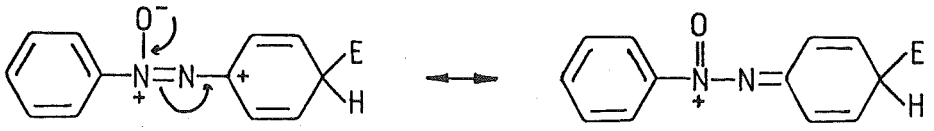
No σ_p^+ value for the phenyl-NNO-azoxy group could be measured in the solvolysis reaction as it proved to be too unreactive in any acetone-water mixture in the range of 100% to 65% acetone. (At 65% acetone-water the corresponding dimethylcarbinyl chloride oiled out of solution). This unreactive nature is not surprising in view of the group's apparent *meta* directing nature towards incoming electrophiles.[94b]

The σ_p^+ value of +0.06 obtained from the solvolysis reaction for the phenyl-ONN-azoxy group is more positive than

that reported by Christoforou (based on positive bromination) by 0.10 units. A similar difference (0.08 units) in the σ_p^+ values was observed between the two reactions for the phenylazo group. This trend is probably not a coincidence, although the similarity in the difference may be. The difference between our σ_p^+ value and that estimated from Miller's chlorination data is greater still.

The σ_m and σ_p values of the phenyl-ONN-azoxy group suggest a value for σ_I of around +0.15 for this substituent.

If the same reasoning is applied in this case as for that argued in the phenylazo system, where the magnitude of the σ_R^+ value is believed to be given by $(\sigma_p^+ - \sigma_p)$, (and not $(\sigma_p^+ - \sigma_I)$), then a figure of -0.20 is obtained. This figure is slightly greater than that obtained for the phenylazo group (-0.16), but the numbers are sufficiently similar to indicate that the σ_R^+ value probably represents the magnitude of the +R effect for the planar phenyl-ONN-azoxy group. Resonance stabilization of electron deficient centres in this configuration had been proposed to involve one of the lone pairs on the azoxy oxygen.



Our results suggest that while this may contribute to some extent, stabilization involving the phenyl group may also be important.

The phenyl-NNO-azoxy group can be considered to be a nitro group in which one of the oxygens has replaced a

phenylimino group, and its properties reflect this nitro character. Its σ_m value is substantially lower than that for the nitro group, (oxygen is more electronegative than nitrogen) but it is still essentially -I -R in character. The σ_m value points to a value for σ_I of about +0.40, which would yield a value for σ_R^- of +0.37. While this is less than that of the nitro group, it is still high enough to put the substituent in the "strong -R" class.

4.22 σ Values for the Hindered Groups

The hindrance to coplanarity was provided by introducing into the molecule methyl groups into the two flanking positions *ortho* to the azo (or azoxy) function. In this way the hindered forms of the phenylazo, 2,6-dimethylphenylazo, t-butylazo and phenyl-ONN-azoxy groups were studied by determining their σ_p^+, and in most cases their σ_p values, by the same methods used for their unhindered analogues. In calculating these constants, allowance was made for the electronic contribution of the two methyl groups by assuming that their electronic effect was independent of the presence of the azo or azoxy function.

The results obtained in this study are summarized below. The corresponding unhindered σ constants are also listed in parentheses, together with the calculated σ_I values for the unhindered groups.

	σ_p	σ_p^+	(σ_I)
Phenylazo	+0.16 (+0.33)	+0.01 (+0.17)	(+0.18)
t-Butylazo	+0.12 (+0.26)	-0.13 (+0.15)	(+0.15)
2,6-Dimethylphenylazo		0.00 (+0.18)	
Phenyl-ONN-azoxy	+0.16 (+0.26)	-0.08 (+0.06)	(+0.15)

The first conclusion reached is that a substantial rate enhancement does occur with the hindered groups, which suggests that the non-planar configuration is likely to be more reactive than the planar one towards electrophilic substitution.

The σ_p values for the hindered phenylazo, t-butylazo and the phenyl-ONN-azoxy groups are now slightly less than their estimated σ_I values, indicating that these groups have lost all their -R character and behave as a weak +R group in this reaction (which only has a weak +R demand for substituents). The magnitude of this +R character is very small, less than 0.05 σ units. This indicates that either the effect of the hindering methyl groups is sufficient to give the non-planar configuration, which is intrinsically a weak +R group, or else that an intermediate configuration between the coplanar and non-planar configurations is reached where a significant -R interaction between the azo and phenyl π systems is just outweighed by the +R interaction of the adjacent nitrogen's lone pair with the electron deficient phenyl π system.

This latter interpretation appears to be more credible than the first. Schaefer and Miraglia[45] in a study of the σ_p values obtained from the pKa's of some 4-substituted-3,5-dimethylbenzoic acids in 50% ethanol-water observed unusual

behaviour with the acetamido substituted derivative. From the pKa data they calculated that the acetamido group was twisted at an angle of 49° to the phenyl ring (not 90° as in the non-planar configuration). This figure may be a little low as it was based on a σ_p value of 0.00 for the acetamido group, rather than -0.07, the currently accepted value, but even so the result suggests that the flanking methyl groups may not encourage a full non-planar configuration. This would mean that in our cases, a -R component may still be present in the hindered systems.

Consideration of the σ_p^+ values also leads to a similar conclusion. Their magnitudes indicate that a considerable increase in the +R character of the groups has occurred for the solvolysis reaction, much more than was expected from the σ_p results. This would suggest that in this reaction there is a considerable non-planar character to the reaction, leading to a greater +R effect.

From the two results, it can be imagined that different degrees of coplanarity (or non-planarity) in the transition state could readily explain the variable resonance (+R) effect exhibited by the phenylazo group in electrophilic substitution reactions. The σ_p^+ for the positive bromination (+0.09) indicates that the transition state is more planar than the hindered solvolysis reaction ($\sigma_p^+ = +0.01$), but less planar than the unhindered solvolysis reaction ($\sigma_p^+ = +0.17$). The transition states for the other electrophilic substitution reactions that report negative σ_p^+ values, and for the side-chain bromination result, must on this basis have even less planar character than the hindered

solvolysis reaction.

The Hammond postulate[95] states that if, during a reaction, two states occur consecutively with nearly equal energy contents, then their interconversion will involve only a small change in molecular structure. Assuming that the azo-compound undergoing reaction in all cases favours a planar configuration, then this predicts that the transition state for the carbinyl chloride solvolysis reaction in the unhindered system is more reactant-like than for positive bromination, which in turn is more reactant-like than the other substitution reactions.

The similarity in activating power between the phenylazo and the 2,6-methylphenylazo substituents in the hindered solvolysis reaction is not surprising considering the lack of direct resonance interaction between the reaction site and the non-reacting phenyl ring. The hindered σ_p^+ values for the two substituents show firstly that four methyl groups are no more effective at forcing a non-planar transition state than two methyl groups. Construction of space-filling models suggest that this indeed is likely to be the case. They also show that indirect stabilization of the intermediate by the orthogonal phenylazo system, is relatively unimportant.

It is also significant that our σ_p^+ values for phenylazo and 2,6-dimethylphenylazo are virtually identical in both the hindered and unhindered systems. This gives

strong support to our previous tentative conclusion (p. 127) that in the latter group the π systems of the aromatic ring and the azo group are not overlapping significantly.

The t-butylazo group shows a larger increase in σ_p^+ values in going from the unhindered to the hindered configurations than any of the other groups. This is very surprising since a similar trend was not observed in the σ_p values based on the benzoic acid ionization. Inspection of space-filling models shows that from a purely steric point of view, the replacement of a phenyl group by a t-butyl group on the far nitrogen should have little effect on the configuration adopted by the azo group. The only explanations that appear to be reasonable are that either the azo system is particularly sensitive to small steric changes in the non-reacting group, or else that the t-butylazo group in its non-planar form is intrinsically a very much more powerful +R group than the phenylazo. Since the actual σ_p^+ value for the hindered t-butylazo group is of comparable magnitude to some of the electrophilic σ_p^+ values for the phenylazo group, we favour the first of these two.

The phenyl-ONN-azoxy group follows the trend established by the other substituents in the hindered configuration. The difference in the σ_p^+ values between the unhindered and hindered configurations is comparable to that observed for the phenylazo substituent, although the actual values are higher in the azoxy case.

The +R effect of the group is normally attributed to the resonance stabilization of the electron deficient reaction site by the azoxy oxygen (see page 37) in a planar

configuration. The rate enhancement observed in the solvolysis reaction due to the hindrance to planarity however, can only be due to the +R stabilization gained by the overlap of the nitrogen lone pair with the electron deficient phenyl ring.

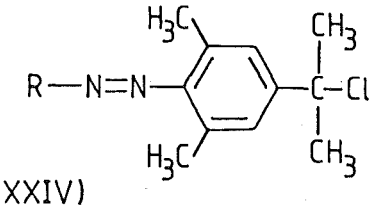
The σ_p^+ value for the positive bromination of azoxybenzene was reported as -0.04, which lies in between our hindered and unhindered solvolysis estimates. The chlorination reaction in acetic acid reported by Miller which lead to an estimate of around -0.2 or greater, which is above the hindered solvolysis estimate.

These results lead us to conclude that a similar situation exists in the electrophilic substitution in azoxybenzene to that observed in the other compounds. We would suggest that the reactions proceed more rapidly in the case of azoxybenzene than azobenzene because of its lower σ_I value and a lesser tendency to remain coplanar in the ground state than that found in azobenzene. These effects appear to be more important than the resonance stabilization involving the azoxy oxygen in the coplanar configuration.

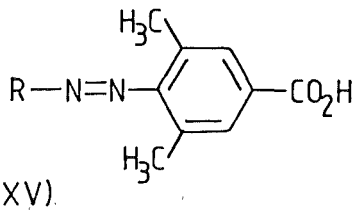
PART II: THE EFFECT OF HINDRANCE TO PLANARITY ON THE TRANSMISSION OF ELECTRONIC EFFECTS THROUGH THE AZO LINKAGE

INTRODUCTION

In Part I the effect of the steric hindrance to coplanarity on the electronic effect of the phenylazo group was investigated by measuring the rates of solvolysis of compounds of type (XXIV) and the pKa's of acids of the type (XXV), where methyl groups were introduced to the ring positions adjacent to the azo linkage.



(XXIV)

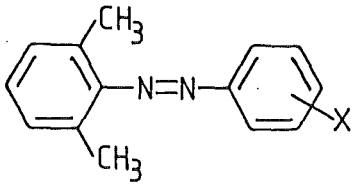


(XXV)

R= C_6H_5 , t-Bu

The results obtained were best explained by assuming that in the unhindered systems the azo group and the aromatic ring were coplanar, but that in the dimethyl analogues (XXIV) and (XXV) the azo linkage was at least partly forced out of the plane of the ring. One possible way of confirming that there has been a loss of coplanarity is to search for signs of a change in the efficiency with which substituent electronic effects, particularly resonance ones, are transmitted from one ring to the other through the azo linkage. The systems studied in Part I were not well suited for this purpose. This was due in part to a general insensitivity of the reactions used to substituent changes at such a remote part of the molecule. A more serious problem, however, was the synthesis of the required compounds bearing a suitable range of substituents.

Instead, a new system was chosen for this study, the ^{13}C n.m.r. chemical shifts of the xylyl ring carbons of 1-arylazo-2,6-dimethylbenzenes (XXVI). This system offered two major advantages over those used in Part I.



(XXVI)

Firstly the system posed few synthetic problems. Secondly, reliable data for the non-methylated analogues was already available, having been reported by Christoforou.[96] These showed at the outset that not only was the system sufficiently sensitive to substituent effects, but that both +R and -R effects could be transmitted from one ring to the other with a fair degree of efficiency.

In recent years, ^{13}C n.m.r. chemical shifts in aromatic systems have been widely used as a means of studying the electronic effects of substituents. This is because studies have shown that in many cases substituent-induced variations in the shifts appear to be directly related to variations in the electron density at the carbon concerned. The carbons most commonly used for this purpose have been the *para* ring ones of monosubstituted benzenes and the terminal (β) ones of ethenyl side-chains. Christoforou found that the side-chain ring carbons in azobenzenes and stilbenes could also be used, with the ring carbon *para* to the azo or ethylene bridge being particularly suitable for the purpose.

Christoforou's results showed that both the inductive and resonance effects could be relayed through the azo group to the non-substituted ring in azobenzenes (as well as to the side-chain in the ethyl arylazocinnamates),[97] but these results by themselves could not establish the

configuration of the azobenzene molecule in solution. Comparison with other systems, such as the stilbenes, or substituted diphenyls, also does not really help to answer this question because the degree of planarity that exists in these systems is also uncertain. For example, there is at least some degree of hindrance to planarity in the diphenyl system as a result of the steric interaction between the *ortho* hydrogens. However comparing Christoforou's azobenzene results with those for the 1-arylazo-2,6-dimethylbenzenes is a more valid and useful exercise in this regard.

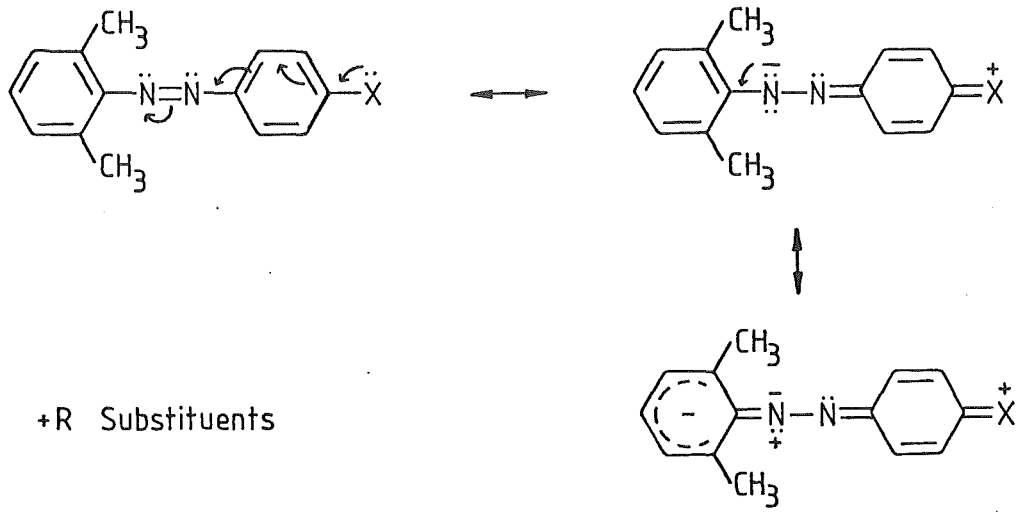
It was considered unlikely that the presence of the two methyl groups would have any major effect on the sensitivity of the xylyl ring carbons to substituent effects except that arising from conformational changes forced by the methyl groups. Christoforou had observed that the presence of the ethenyl ester side-chain in the 3-and 4-arylazo ethyl cinnamates did not change the sensitivity of the C3 and C4 ring carbons in the corresponding azobenzenes. On the other hand, any substantial loss of planarity of the system, such as might arise from steric interaction between one of the introduced methyl groups and the more distant nitrogen of the azo linkage, might well have an effect on the sensitivity of the xylyl ring carbons to substituent effects.

The efficiency of transmission of inductive effects would not be predicted to change much as a consequence, since it is now accepted that their dominant influence arises from a field effect, (although the mechanism by

which this effect is relayed may well be different in the planar and non-planar situations).

The effect of loss, or partial loss, of planarity on the transmission of resonance effects, however, should be much greater since this effect is relayed by different mechanisms in the planar and non-planar configurations. In a planar configuration, resonance effects are transmitted by through-conjugation of the molecules π systems.

In a non-planar configuration, such direct through-conjugation is lost, but indirect relay from the far nitrogen to the xylyl ring is possible.



+R Substituents

-R Substituents

For +R substituents, relay to the xylyl ring is achieved by a resonance mechanism involving the lone pair, while for -R ones, only an inductive transfer mechanism is possible. This would suggest that the response of resonance effect to loss of planarity might be different for the two classes of substituents.

This system should therefore provide a convenient method to study the transmission of substituent electronic effects through the hindered phenylazo linkage. Accordingly, a series of 20 compounds covering a suitable range of substituents was prepared. The ^{13}C n.m.r. spectra of all compounds were then determined under the same conditions (including the same instrument) as those used by Christoforou.

2. EXPERIMENTAL

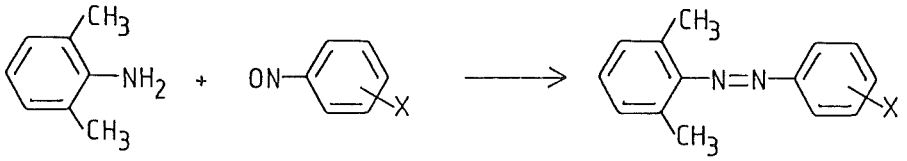
2.0 Introduction

The general experimental conditions described in part I also apply here. Those compounds that were oils were distilled in a Kugelrohr apparatus under high vacuum.

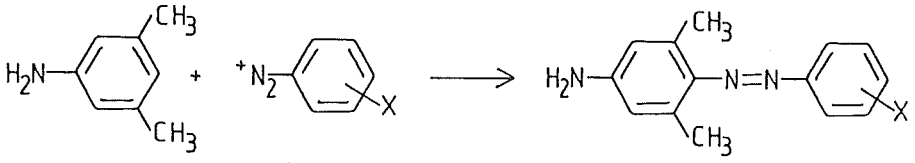
Carbon-13 n.m.r. spectra were obtained for 0.4 M solutions in deuterochloroform, with tetramethylsilane as the internal standard.

2.1 Preparation of the Substituted 2,6-Dimethylazobenzenes

Three synthetic methods were used. These are summarised below.



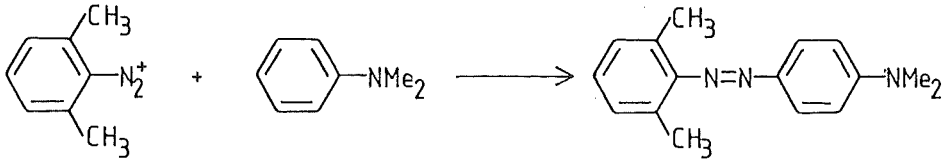
X = H, 3-Me, 4-Me, 4-Ac, 4-CO_2Et



X = 3-OMe, 4-OMe, 4-F, 3-Cl, 4-Cl, 3-Br, 4-Br, 3-CF_3, 4-CF_3, 3-Ac, 3-CO_2Me, 3-CN, 4-CN, 3-NO_2, 4-NO_2

(1) H^+/ H_2O / $NaNO_2$

(2) H_3PO_2



2.11 Condensation of Substituted Nitrosobenzenes with 2,6-Dimethylaniline

The preparation of nitrosobenzene, 4-nitrosotoluene, ethyl 4-nitrosobenzoate and 4-nitrosoactetophenone have been described previously. 3-Nitrosotoluene was prepared in 65% yield by the general method of Barrow and Thorneycroft.[83]

The literature[74] method described below for 2,6-dimethylazobenzene was also used for the other members of the series prepared in this manner.

The yields in most cases were very low.

2,6-Dimethylazobenzene

Nitrosobenzene (1.6 g) in ethanol (15 ml), was added to a solution of 2,6-dimethylaniline (2.0 ml) in acetic acid (5 ml). The mixture was heated on a steam bath for 30 min, then worked up in the normal manner. The crude product was purified on a silica Chromatotron plate to give 2,6-dimethylazobenzene (0.92 g), as a red oil. ν_{max} (liquid film) 3175, 2970 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.38, Me_2; 7.03, H3, H4, H5; 7.33-7.53, m, 3H, phenyl protons; 7.73-7.93, m, 2H, phenyl protons.

2,3',6-Trimethylazobenzene

3-Nitrosotoluene (2 g) on reaction with 2,6-dimethylaniline gave a red oil which distilled at 135°/0.5 mm Hg to give 2,3',6-trimethylazobenzene (0.80 g) (Found C, 80.5; H, 7.3; N, 12.6. $C_{15}H_{16}N_2$ requires C, 80.3; H, 7.2; N, 12.5%). ν_{max} (liquid film) 2980, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.37, Me_2; 2.47, CH_3; 7.03, H3, H4, H5; 7.20-7.75, m, H2', H4', H5', H6'.

2,4'6-Trimethylazobenzene

4-Nitrosotoluene (2 g) on reaction with 2,6-dimethylaniline gave 2,4',6-trimethylazobenzene (0.40 g), as a red oil. ν_{max} (liquid film) 2980, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.33, Me_2; 2.40, CH_3; 6.98, H3, H4, H5; 7.16, 7.67, J_{AB} 10Hz, H2', H3', H5', H6'. (^1H n.m.r. agrees with that in the literature [98]).

4'-Acetyl-2,6-dimethylazobenzene

Crude 4-nitrosoacetophenone (13 g) and 2,6-dimethylaniline (5 ml) were condensed to give a red oil which on distillation at 175°/0.5 mm Hg yielded 4'-acetyl-2,6-dimethylazobenzene (0.41 g) (Found C, 76.6; H, 6.5; N, 11.2. $C_{16}H_{16}N_2O$ requires C, 76.2; H, 6.4; N, 11.1%). ν_{max} (liquid film) 3000, 2950, CH; 1690 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 2.43, Me_2; 2.60, CH_3, 7.07, H3, H4, H5; 7.87, 8.07, J_{AB} 9Hz, H2', H3', H5', H6'.

4'-Carboethoxy-2,6-dimethylazobenzene

Ethyl 4-nitroso benzoate (2 g) on reaction with 2,6-dimethylaniline gave a red oil which was distilled at 165°/0.5 mm Hg to give 4'-carboethoxy-2,6-dimethylazobenzene (0.27 g) (Found C, 72.1; H, 6.5; N, 9.9. $C_{17}H_{18}N_2O_2$ requires C, 72.3; H, 6.4; N, 9.9%). ν_{max} (liquid film) 3000, 2950, CH; 1725 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 1.40, t, J7Hz, CH_3; 2.40, Me_2; 4.33, t, J7Hz, CH_2; 7.03, H_3, H4, H5; 7.80, 8.13, J_{AB} 8Hz, H2', H3', H5', H6'.

2.12 Coupling Reaction of Substituted Benzenediazonium Salts to 3,5-Dimethylaniline

The method shown below for 2,6-dimethyl-4'-methoxyazobenzene was also adopted for the other members of the series. In all cases 6.2×10^{-3} mol of the substituted aniline was used.

2,6-Dimethyl-4'-methoxyazobenzene

4-Methoxyaniline (0.76 g, 6.2×10^{-3} mol), dissolved in concentrated hydrochloric acid (1 ml) and water (2 ml) was diazotised with a solution of sodium nitrite (0.45 g) in water (10 ml) at 0-5°. A solution of sodium acetate (2 g), water (10 ml), 3,5-dimethylaniline (0.75 g) and ethanol (10 ml) was then added with stirring. The mixture was allowed to stand at 20° for 2 h, then extracted into dichloromethane. The dichloromethane layer was separated, washed, dried and the solvent removed under reduced pressure to give crude intermediate. This was then heated on a steam bath with concentrated hydrochloric acid (1.5 ml) and water (10 ml) for 15 min, before being cooled. The crude 4-amino-2,6-dimethyl-4'-methoxyazobenzene hydrochloride was diazotised with sodium nitrite (0.54 g) in water (10 ml) at 0-5° and 30% hypophosphorous acid (30 ml) was added. The mixture was kept at 4° for 20 h and then diluted with dichloromethane. The organic layer was washed with water and the solvent removed under reduced pressure. The residue was purified on a silica Chromatotron plate to give 2,6-dimethyl-4'-methoxyazobenzene (0.21 g), as a red oil. ν_{max} (liquid film) 2960, 2930 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.33, Me_2;

3.83, OMe; 6.98, H3, H4, H5; 6.88, 7.80, J_{AB} 9Hz, 4H, H2', H3', H5', H6'. (Spectral properties are similar to those in the literature[99]).

2,6-Dimethyl-3'-methoxyazobenzene

3-Methoxyaniline (0.76 g) gave a red oil which on distillation at 120-130°/0.5 mm Hg yielded 2,6-dimethyl-3'-methoxyazobenzene (0.20 g). (Found C, 74.9; H, 6.9; N, 11.5. $C_{15}H_{16}N_2O$ requires C, 75.0; H, 6.7; N, 11.7%). ν_{max} (liquid film) 2990 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.35, Me_2; 3.83, OMe; 7.02, H3, H4, H5; 7.17-7.53, m, H2', H4', H5', H6'.

2,6-Dimethyl-4'-fluoroazobenzene

4-Fluoroaniline (0.69 g) gave a red oil which on distillation at 130°/0.5 mm Hg yielded 2,6-dimethyl-4'-fluoroazobenzene (0.33 g). (Found C, 74.2; H, 5.8; N, 12.2. $C_{14}H_{13}FN_2$ requires C, 73.7; H, 5.7; N, 12.3%). ν_{max} (liquid film) 3000, 2960 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.37, Me_2; 7.03, H3, H4, H5; 6.98-7.27, m, 2H, phenyl protons; 7.72-7.97, m, 2H; phenyl protons.

3'-Chloro-2,6-dimethylazobenzene

3-Chloroaniline (0.79 g) gave a red oil which on distillation at 200°/0.5 mm Hg yielded 3'-chloro-2,6-dimethylazobenzene (0.36 g). (Found C, 68.3; H, 5.3; N, 11.6. $C_{14}H_{13}ClN_2$ requires C, 68.7; H, 5.4; N, 11.5%). ν_{max} (liquid film) 3075, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.38, Me_2; 7.02, H3, H4, H5; 7.26-7.63, m, 4H, H2', H4', H5', H6'.

4'-Chloro-2,6-dimethylazobenzene

4-Chloroaniline (0.79 g) gave a red oil which on distillation at 145°/0.5 mm Hg yielded 4'-chloro-2,6-dimethylazobenzene (0.38 g). (Found C, 69.0; H, 5.6; N, 11.5. $C_{14}H_{13}ClN_2$ requires C, 68.7; H, 5.4; N, 11.5%). ν_{max} (liquid film) 3000, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.38, Me_2; 7.05, H3, H4, H5; 7.43, 7.82, J_{AB} 9Hz, 4H, H2', H3', H5', H6'.

3'-Bromo-2,6-dimethylazobenzene

3-Bromoaniline (1.07 g) gave a red oil which on distillation at 165-185°/0.5 mm Hg yielded 3'-bromo-2,6-dimethylazobenzene (0.25 g) (Found C, 58.3; H, 4.6; N, 9.8. $C_{14}H_{13}BrN_2$ requires C, 58.2; H, 4.5; N, 9.7%). ν_{max} (liquid film) 3000, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.38, Me_2; 7.03, H3, H4, H5; 7.28-7.95, m, H2', H4', H5', H6'.

4'-Bromo-2,6-dimethylazobenzene

4-Bromoaniline (1.07 g) gave a red oil which on distillation at 150°/0.5 mm Hg yielded 4'-bromo-2,6-dimethylazobenzene (0.25 g) (Found C, 57.9; H, 4.6; N, 9.6. $C_{14}H_{13}BrN_2$ requires C, 58.2; H, 4.5; N, 9.7%). ν_{max} (liquid film) 2980, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.38, Me_2; 7.05, H3, H4, H5; 7.67, H2', H3', H5', H6'.

2,6-Dimethyl-3'-trifluoromethylazobenzene

3-Trifluoromethylaniline (1.0 g) gave a red oil which on distillation at 130-135°/0.5 mm Hg yielded 2,6-dimethyl-3'-trifluoromethylazobenzene (0.30 g) (Found C, 65.0; H, 4.7; N, 10.2. $C_{15}H_{13}F_3N_2$ requires C, 64.7; H, 4.7; N, 10.1%). ν_{max} (liquid film) 3000, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ

2.43, Me_2; 7.05, H3, H4, H5; 7.38-8.08, m, H2', H4', H5', H6'.

2,6-Dimethyl-4'-trifluoromethylazobenzene

4-Trifluoromethylaniline hydrochloride (1.0 g) gave a red oil which on distillation at 105-115°/0.5 mm Hg yielded 2,6-dimethyl-4'-trifluoromethylazobenzene (0.15 g). ν_{max} (liquid film) 3000, 2950 cm^{-1}, CH. ^1H n.m.r. (CCl_4) δ 2.37, Me_2; 7.03, H3, H4, H5; 7.70, 7.93, J_{AB} 9Hz, H2', H3', H5', H6'. (Spectral properties are similar to those in the literature[99]).

3'-Acetyl-2,6-dimethylazobenzene

3-Aminoacetophenone (0.84 g) gave a red solid which on distillation at 150°/0.5 mm Hg yielded 3'-acetyl-2,6-dimethylazobenzene (0.68 g), m.p. 33-36° (Found C, 76.0; H, 6.5; N, 10.9. $C_{16}H_{16}N_2O$ requires C, 76.2; H, 6.4; N, 11.1%). ν_{max} (liquid film) 3000, 2950, CH; 1690 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 2.42, Me_2; 2.63, $COCH_3$; 7.00, H3, H4, H5; 7.30-8.46, m, H2', H4', H5', H6'.

3'-Carbomethoxy-2,6-dimethylazobenzene

Methyl 3-aminobenzoate (0.94 g) gave a red oil which on distillation at 190-200°/0.5 mm Hg yielded 3'-carbomethoxy-2,6-dimethylazobenzene (0.52 g) (Found C, 71.8; H, 6.0; N, 10.4. $C_{16}H_{16}N_2O_2$ requires C, 71.6; H, 6.0; N, 10.4%). ν_{max} (liquid film) 2950, CH; 1725 cm^{-1}, C=O. ^1H n.m.r. (CCl_4) δ 2.42, Me_2; 3.92, CH_3; 7.07, H3, H4, H5; 7.37-8.50, m, H2', H4', H5', H6'.

3'-Cyano-2,6-dimethylazobenzene

3-Cyanoaniline (0.65 g) gave light orange crystals which were recrystallized from pentane to give 3'-cyano-2,6-dimethylazobenzene (0.40 g), m.p. 90.5-91.5° (Found C, 76.7; H, 5.7; N, 17.7. $C_{15}H_{13}N_3$ requires C, 76.6; H, 5.6; N, 17.8%). ν_{max} (Nujol) 2250 cm^{-1}, CN. ^1H n.m.r. (CCl_4) δ 2.43, Me_2; 7.08, H3, H4, H5; 7.40-8.13, m, H2', H4', H5', H6'.

4'-Cyano-2,6-dimethylazobenzene

4-Cyanoaniline (0.65 g) gave light red crystals which were recrystallized from pentane to give 4'-cyano-2,6-dimethylazobenzene (0.57 g), m.p. 70-71.5° (Found C, 76.5; H, 5.8; N, 17.7. $C_{15}H_{13}N_3$ requires C, 76.6; H, 5.6; N, 17.8%). ν_{max} (Nujol) 2250 cm^{-1}, CN. ^1H n.m.r. (CCl_4) δ 2.43, Me_2; 7.12, H3, H4, H5; 7.77, 7.93, J_{AB} 8 Hz, H2', H3', H5', H6'.

2,6-Dimethyl-3'-nitroazobenzene

3-Nitroaniline (0.86 g) gave light orange crystals which were recrystallized from pentane to give 2,6-dimethyl-3'-nitroazobenzene (0.16 g), m.p. 95° (Found C, 65.5; H, 4.9; N, 16.1. $C_{14}H_{13}N_3O_2$ requires C, 65.9; H, 5.1; N, 16.5%). ν_{max} (Nujol) 1520, 1330 cm^{-1}, NO_2. ^1H n.m.r. (CCl_4) δ 2.45, Me_2; 7.05, H3, H4, H5; 7.43-8.63, m, H2', H4', H5', H6'.

2,6-Dimethyl-4'-nitroazobenzene

4-Nitroaniline (0.86 g) gave purple crystals which were recrystallized from light petroleum to give 2,6-dimethyl-4'-nitroazobenzene (0.18 g), m.p. 66° (Found C, 65.7; H, 5.3; N, 16.2. $C_{14}H_{13}N_3O_2$ requires C, 65.9, H, 5.1; N, 16.5%).

ν_{max} (Nujol) 1515, 1325 cm^{-1}, NO_2. ^1H n.m.r. (CCl_4) δ 2.43, Me_2; 7.08, H3, H4, H5; 7.90, 8.33, J_{AB} 10Hz, H2', H3', H5', H6'.

2.13 Preparation of 2,6-Dimethyl-4'-dimethylaminoazobenzene

2,6-Dimethylbenzenediazonium chloride was coupled to N,N-dimethylaniline and worked up by the method described by Ryan.[108] The crude product on purified on a silica Chromatotron plate and recrystallized from light petroleum to give orange crystals (20%), m.p. 118-119° (lit. 103.5-104.5°, from benzene[109]). (Found $M^{+\cdot}$, 253.1570. Calc. for $C_{16}H_{19}N_3$: $M^{+\cdot}$, 253.1579). ^1H n.m.r. (CCl_4) δ 2.30, Me_2; 3.00, NMe_2; 6.93, H3, H4, H5; 6.57, 7.65, J_{AB} 9Hz, H2', H3', H5', H6'. ^{13}C n.m.r. spectra in $CDCl_3$ or DMSO failed to give a spectum that was consistent with 2,6-dimethyl-4'-dimethylamino-azobenzene. For this reason it was not used in the results or discussion.

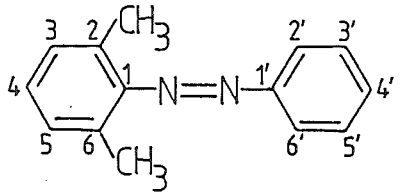
2.2 Assignment of Chemical Shifts

The assignment of the chemical shift resonances was achieved without any major difficulty, (except for the 4'-dimethylamino compound). The substituted carbon ring was assigned by comparison with the shifts of the corresponding substituted azobenzenes reported by Christoforou and Happer.[96] The dimethyl substituted carbon ring was assigned by means of the additivity effect of the dimethyl groups and on peak intensity.

In only two cases was an overlap of shifts observed, those being the C3 and C4 carbons for the 3'-cyano and 3'-nitro derivatives.

3. RESULTS

The ^{13}C n.m.r. chemical shifts of all the carbon atoms of the substituted 2,6-dimethylazobenzenes studied are listed on the following page. In all cases the chemical shift (δ) is quoted in p.p.m. downfield from tetramethylsilane. Missing figures indicate that peaks were not observed. In all cases only one isomer (presumably the *trans* isomer) was observed.



Substituent	Carbon 1'	2'	3'	4'	5'	6'	1	2	3	4	Me_2	X		
H	152.83	122.51	129.10	130.96	129.10	122.51	151.52	130.61	129.10	128.09	18.76			
3'-OMe	154.02	105.81	160.35	117.44	129.79	116.60	151.41	130.57	129.10	128.13	18.75	55.42		
4'OMe	147.21	124.31	114.16	162.10	114.16	124.31	151.66	130.27	129.00	127.54	18.65	55.56		
3'-Me	152.93	122.90	139.01	131.75	128.91	119.87	151.66	130.42	129.06	127.96	18.70	21.35		
4'-Me	151.00	122.53	129.72	141.52	129.72	122.53	151.68	130.43	129.07	127.85	18.68	21.43		
4'-F		124.71 124.27	116.59 116.47	170.80 158.20	116.59 116.47	124.71 124.27	151.23	130.78	129.17	128.25	18.85			
3'-Cl	153.66	121.88	135.18	130.64	130.12	121.53	150.85	131.25	129.25	128.72	19.04			
4'-Cl	151.03	123.72	129.33	136.91	129.33	123.72	151.21	130.96	129.20	128.48	18.94			
3'-Br	153.75	124.46	123.14	133.54	130.42	122.37	150.84	131.25	129.25	128.75	19.04			
4'-Br	151.53	123.97	132.32	125.39	132.32	123.97	151.02	131.04	129.23	128.56	18.99			
3'-Ac	152.91	122.93	138.22	130.25	129.42	126.10	150.96	131.17	129.28	128.73	19.04	194.77	26.74	
4'-Ac	155.17	122.50	129.37	138.42	129.37	122.50	150.91	131.53	129.37	120.09	19.18	194.92	26.76	
3'-CO_2Me	152.84	124.11		131.67	131.39	126.07	151.02	131.20	129.24	128.66	19.04	166.51	52.31	
4'CO_2Et	155.26	122.23	130.60	132.21	130.60	122.23	150.97	131.44	129.33	128.95	19.14	166.01	61.23	14.34
3'-CF_3	152.87	119.51		127.23	129.72	125.60	150.82	131.49	129.38	129.04	19.13			
4'-CF_3	154.60	122.70	126.34		126.34	122.70	150.89	131.51	129.40	129.11	19.14			
3'-CN	152.76	125.72		133.68	130.10	127.00	150.37	131.87	129.45	129.45	19.33	113.46		
4'CN	154.67	122.98	133.24	118.44	133.42	122.98	150.48	132.06	129.48	129.62	19.37	113.94		
3'-NO_2	153.26	116.94	129.33	124.85	129.98	128.46	150.29	132.07	129.50	129.50	19.42			
4'NO_2	155.85	123.00	124.75		124.75	123.00	150.49	132.37	129.57	129.92	19.51			

4. DISCUSSION

Before considering the results obtained in the previous section, it is appropriate at this point to briefly review some aspects of the current thinking on the interpretation of the changes in ^{13}C n.m.r. chemical shifts in unsaturated, especially conjugated unsaturated, side-chains and the effect that ring substituents have on them. A more detailed treatment of the topic is to be found in a recent review by Craik and Brownlee.[100]

To date the most widely studied aromatic side-chain systems have been the styrene and α-carbonyl systems. Of the two, the former represents a closer analogy with our system, in that the functional group involved has a negligible dipole moment. It has also been the most thoroughly investigated of the two.

It is generally agreed that the changes in the ^{13}C n.m.r. chemical shifts of side-chain carbons in systems of these types that occur as a result of introducing substituents into the *meta* or *para* positions of the ring are directly related to the magnitudes of their inductive and resonance effects. In assessing the relative contributions of each of these on a quantitative basis, the observed shifts are best analysed, at least in the first instance, by the Dual Substituent Parameter (DSP) equation

$$SCS(X) = \rho_I \sigma_I^X + \rho_R \sigma_R^X$$

In the above equation, SCS(X), the so-called substituent chemical shift of the introduced substituent X, is defined as the change in chemical shift observed that results from its introduction, i.e.

$$SCS(X) = \delta^{13}C(X) - \delta^{13}C(H)$$

In the DSP equation in its accepted form the σ_R parameter used is normally either σ_R^o, σ_R^{BA}, σ_R^+ or σ_R^-, depending on which scale fits the data best. In correlating ^{13}C data of side-chains it has often proved necessary to correlate the data for +R and -R substituents independently as different σ_R scales are sometimes required for the two types of substituents. Care should also be taken that substituent parameters (σ_I and σ_R values) appropriate to the solvent used are chosen.

DSP analysis of SCS data yields optimum values of ρ_I and ρ_R, and from the type of σ_R scale needed, a guide to the strength of any resonance interaction of the carbon whose shift is being investigated is obtained. The ρ_I and ρ_R values may be regarded as a measure of the efficiency with which the appropriate substituent effects are relayed to the probe site.

4.1 Inductive Effects

The efficiency with which the electronic effects of substituents are transmitted through a system will depend on the mechanism involved. For resonance effects this is quite straightforward in that it is purely a consequence of π orbital overlap, but for the case of inductive effects a number of different relay mechanisms have been proposed. It is very probable that more than one may be involved, and there is some question as to whether their relative contributions to chemical shifts are the same as in chemical reactions.

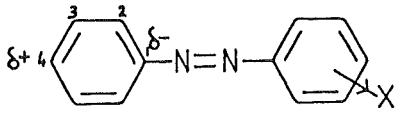
Reynolds[3] has considered the possible modes of transmission of substituent inductive effects to the probe site and attempted to assess their relative contributions to the total. For the case of ^{13}C n.m.r. chemical shifts where π systems are involved, he considers that the most important inductive mechanism to be via the polarization of the π system induced by the field effect of the substituent. In cases where two independent π systems capable of conjugative interaction are involved, this effect will have two components.

(i) Direct field-induced polarization of each individual π system.

(ii) Field-induced π-electron transfer from one group to the other. Of the two, the second is particularly important in our case since it allows efficient transmission of inductive effects to remote sites in conjugated aromatic systems.

Brownlee,[101] in a study of the ^{13}C n.m.r. chemical shifts of side-chain carbonyl carbons, reached a similar conclusion, although he used slightly different terminology. He referred to the two types of transmission as "localized" and "extended" polarization respectively. In the following discussion we will use the latter's terminology.

In systems such as ours, localized polarization predicts that as a result of the independent polarization of a side-chain π system, (a phenyl group in our case), the effect a substituent exerts on the nearest and farthest carbons of the side-chain should be opposite. This means, for example, that the introduction of an electron withdrawing substituent into our system should result in a downfield shift at C4 and an upfield shift at C1 as it decreases the electron density at the former and increases it on the latter. Any accompanying



extended polarization should further decrease the electron density at C4 but it is difficult to judge what effect it would have on C1. Such an effect is always observed in the double bond of styrenes[102] and has been noted in a number of cases where side-chain phenyl groups are involved, including the diphenyls,[103] terphenyls[104] and Christoforou's azobenzenes and stilbenes.[96]

Since extended polarization requires the presence of a conjugated π system, and this, in turn requires an approximately coplanar molecule, then in the azobenzene system, any factor that discourages coplanarity should also reduce the contribution that extended polarization makes to the overall inductive effect. Localized polarization should be less affected. One might predict therefore, that if the introduction of the two flanking methyl groups into the azobenzenes were to result in a significant loss of coplanarity of the system as a whole, then not only should ρ_R at C2 and C4 be affected, but there could also be a decrease in ρ_I at C4 and especially its value relative to C2.

We are now in a position to consider the results obtained in our ^{13}C n.m.r. study in terms of these factors, concentrating in the first instance on the series where the introduced substituent is *meta* to the xylylazo side-chain. In this series inductive effects are expected to dominate.

The relevant SCS data are summarised in Table 21, together with the corresponding data for the unmethylated azobenzene analogues.

Because of the distances involved the effect of the substituents on the SCS values in many cases is rather small; and it should be borne in mind throughout this discussion that the reported shifts have an accuracy of at best ±0.05 ppm.

A preliminary inspection of the data shows that

(a) the effect of substituents on the SCS values for C1 and C4 are opposite, and

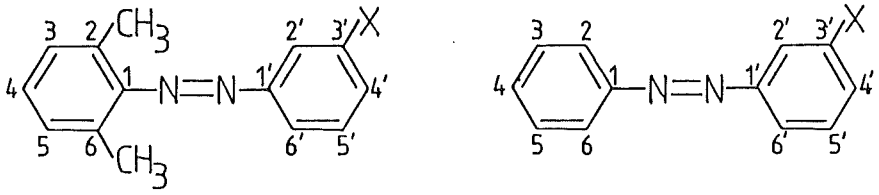
(b) the overall sensitivity of the various carbons to substituent effects is greater, (in most cases, much greater) than those for the corresponding azobenzene series.

The result (a) is as expected, but (b) is not. The increased overall sensitivity would seem greater than could be accounted for on the basis of any electronic effect arising from the presence of the two methyl groups. The logical alternative explanation is that the changes arise from differences in the geometry of the system as a result of their presence. That some change in the geometry is possible is confirmed by their effect on σ_p^+ for the phenylazo and related groups in Part I.

The variations in inductive effects can be put on a more quantitative basis by analysing the data using the DSP equation. The results of these analyses are given in Table 22. All correlations are made using the σ_R^o parameter since the substituent X is *meta* to the side-chain.

The DSP analyses give low $\lambda (=\rho_R/\rho_I)$ values for all carbons, which suggests that correlations using Hammett σ_m values may

Table 21. ^{13}C n.m.r. Substituent Chemical Shifts for Side-Chain Carbons in *meta*-Substituted 2,6-Dimethylazobenzenes and Azobenzenes



Substituent	2,6-Dimethylazobenzenes					Azobenzenes			
X	C1	C2	C3	C4	CMe	C1	C2	C3	C4
H	151.52	130.61	129.10	128.09	18.76	152.72	122.89	129.09	130.98
Me	0.14	-0.19	-0.04	-0.13	-0.06	0.07	-0.05	-0.04	-0.13
OMe	-0.11	-0.04	0.00	0.04	-0.01	-0.14	-0.04	-0.04	0.02
CO_2Me	-0.55	0.59	0.14	0.57	0.28	-0.21	0.14	0.03	0.41
Ac	-0.56	0.56	0.18	0.64	0.28	-0.25	0.12	0.09	0.50
Cl	-0.67	0.64	0.15	0.63	0.28	-0.28	0.19	0.05	0.51
Br	-0.68	0.64	0.15	0.66	0.28	-0.35	0.19	0.05	0.52
CF_3	-0.70	0.88	0.28	0.95	0.37	-0.30	0.28	0.14	0.74
CN	-1.15	1.26	0.35	1.36	0.57	-0.55	0.36	0.19	1.06
NO_2	-1.23	1.46	0.40	1.41	0.66	-0.53	0.43	0.16	1.14

Table 22. DSP Analyses of the Ring Carbon SCS Values for the *meta*-Substituted 2,6-Dimethylazobenzenes and Azobenzenes

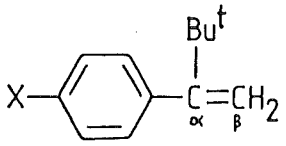
	2,6-Dimethylazobenzenes				Azobenzenes			
Carbon	C1	C2	C3	C4	C1	C2	C3	C4
ρ_I	-1.7	1.9	0.5	1.9	-0.8	0.5	0.2	1.5
ρ_R	-0.6	1.1	0.3	1.0	-0.2	0.3	0.2	0.8
λ	0.4	0.6	0.6	0.5	0.2	0.6	1.0	0.5
f	0.11	0.10	0.12	0.10	0.15	0.19	0.29	0.11
ρ^{meta}	-1.61	+1.92	0.52	1.90	-0.69	0.58	0.27	1.53

yield a more reliable measure of ρ_I. These have therefore been evaluated and listed at the bottom of the Table. The correlations between the data and σ_m, as judged by the f values obtained, are invariably better than the DSP correlations, supporting such an assumption.

The results show quite clearly that for all ring carbons ρ_I is <u>greater</u> in the xylylazo series than in the phenylazo one. This is somewhat unexpected since any changes were expected to result in lower ρ_I values because of partial loss of extended polarization, commonly regarded as the major transmission pathway for inductive effects in systems of this type. The biggest surprise however is the magnitude by which the ρ_I values have increased. Although the magnitude of the increase at C1, especially relative to C4 is not unexpected, since any fall off in extended polarization not only decreases the overall charge on C4 but it also removes a pathway by which any electron density built up on C1 as a result of localized polarization can be dispersed.

The most reasonable interpretation of the results is that, as a result of changes in the orientation of the xylyl ring with respect to the field generated by the substituent dipole, the sensitivity of the shifts of the various ring carbons to localized polarization has been considerably enhanced. This enhancement, however, may be to some extent offset by a loss of extended polarization, a transmission pathway that, as we noted earlier, is likely to affect C4 more than the other ring carbons.

The trend observed conflicts with that reported by Reynolds[105] in his study of the 4-X-α-t-butylstyrenes.



When the results for this system are compared with those of the corresponding styrenes, it is found that ρ_I for both Cα and Cβ had decreased, the former only slightly, the latter by about 50%. However the geometries of his and our systems are somewhat different, and if the magnitude of the localized polarization is strongly geometry-dependent, then the results may not be all that out of line.

4.2 Resonance Effects

Electron transfer by a resonance mechanism is, in general, reasonably well understood. However when applied to phenomena such as ^{13}C n.m.r. chemical shifts of conjugated side-chains, some of the resonance effects are not as easily explained. For example, DSP analyses of some carbon shifts (e.g. Cα of styrenes) yield negative values for both ρ_I and ρ_R.

"Reverse" inductive effects, as we have already seen, can be explained in terms of localized polarization, but no satisfactory explanation is available for "reverse" resonance effects. Christoforou found that for both azobenzenes and stilbenes, negative ρ_R values were obtained at Cl in both the *meta* and *para* series. Our results show that this is also the case for the xylylazo system.

We have previously investigated the operation of inductive effects in our system by considering the effect of

meta ring substituents on the side-chain chemical shifts. In these situations the small resonance contribution observed can be considered to arise from some "leakage" process. Such leakage appears to be approximately independent of electron demand (σ_m is widely recognised as carrying a reaction independent resonance component) and when recognised this can therefore be allowed for.

To study resonance effects, investigation of *para* substituent effects are required. Like resonance effects in *meta* series, the inductive contribution in the case of *para* substituents is constant and can be allowed for, but unlike them, cannot be evaluated in an independent system. Furthermore, the inductive component in σ_p is often a much greater contributor to the total substituent effect than is the resonance one to σ_m.

For reactivity studies, the inductive component to σ_p is usually estimated by assuming $\rho_I^{meta} = \rho_I^{para}$. For the case of ^{13}C n.m.r. chemical shift studies this equality may not be taken for granted. It has certainly been shown to be incorrect for the case of *meta* and *para* ring carbons of monosubstituted benzenes, although anisotropic effects may be involved here. On the other hand, in systems where the substituent and probe site are further apart, there is some evidence that $\rho_I^{meta} = \rho_I^{para}$. Christoforou's results for the stilbenes and azobenzenes systems, were consistent with this, at any rate.

If we make this assumption, then the SCS value can be easily resolved into inductive and resonance components. As a preliminary to this, let us compare the results for DSP

analyses of our *para* substituted 2,6-dimethylazobenzenes with those for Christoforou's azobenzenes. The corresponding SCS values are given in Table 23, and the DSP analyses in Table 24.

It can be seen that the discrepancies between the ρ_I and ρ^{meta} values are not great, especially for C2, C3 and C4 carbons, and are in fact of similar magnitude to those reported in the stilbenes.[96] It therefore does not appear unreasonable to assume that $\rho_I^{para} \approx \rho_I^{meta} \approx \rho^{meta}$ in our 2,6-dimethylazobenzene series.

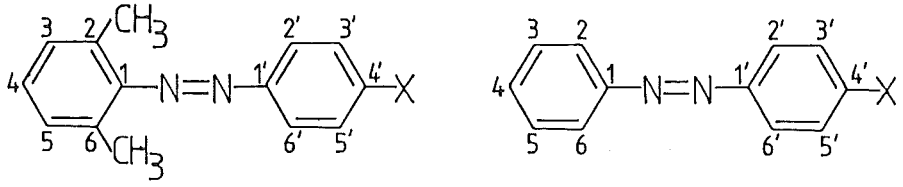
The contributions that the resonance effects of the substituents make to the observed shifts can be estimated by subtracting the inductive contribution ($\sigma_I \times \rho^{meta}$) from the observed SCS values. (A list of σ_I values for our substituents applicable in $CDCl_3$ solvent is available[106]).

These resonance contributions are listed in Table 25.

A preliminary examination shows that the approach appears to be successful for all carbons except Cl in both series, where for some -R substituents the change in chemical shift lies in the wrong direction. It is conceivable that ρ_I^{para} may be significantly less than ρ_I^{meta} for this carbon, but it is more likely that there are substituent effects other than simple electronic ones that are influencing the shifts at this position.

The most striking feature of the results for the other carbons is that the introduction of the two methyl groups does not appear to have resulted in the expected fall off in the effect of resonance on the chemical shift. On the contrary, for C2, and C3, it has considerably enhanced it, while for C4, there is little change. At this point in the

Table 23. ^{13}C n.m.r. Substituent Chemical Shifts for Side-Chain Carbons in *para*-Substituted 2,6-Dimethylazobenzenes and Azobenzenes

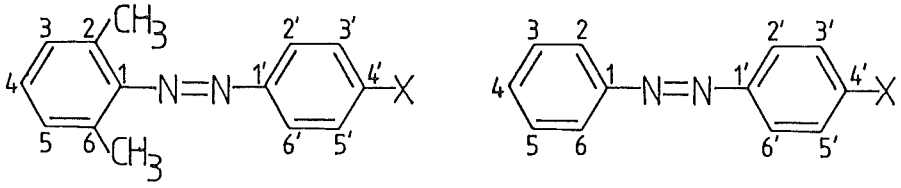


Substituent	2,6-Dimethylazobenzenes					Azobenzenes			
X	C1	C2	C3	C4	CMe	C1	C2	C3	C4
H	151.52	130.61	129.10	128.09	18.76	152.72	122.89	129.09	130.98
OMe	0.14	-0.34	-0.10	-0.55	-0.11	0.09	-0.30	-0.05	-0.62
Me	0.16	-0.18	-0.03	-0.24	-0.08	0.10	-0.13	-0.05	-0.30
F	-0.29	0.17	0.07	0.16	0.09	-0.19	-0.05	0.00	0.02
Cl	-0.31	0.35	0.10	0.39	0.18	-0.19	0.07	0.05	0.27
Br	-0.50	0.43	0.13	0.47	0.23	-0.19	0.09	0.05	0.31
CF_3	-0.63	0.90	0.30	1.02	0.38	-0.26	0.32	0.12	0.85
CO_2Et	-0.55	0.83	0.23	0.86	0.38	-0.15	0.27	0.08	0.67
Ac	-0.61	0.92	0.27	1.00	0.42	-0.33	0.27	0.08	0.77
CN	-1.04	1.45	0.38	1.53	0.61	-0.37	0.45	0.16	1.22
NO_2	-1.03	1.76	0.47	1.83	0.75	-0.30	0.54	0.20	1.42

Table 24. DSP Analyses of the Ring Carbon SCS Values for *para*-Substituted 2,6-Dimethylazobenzenes and Azobenzenes

	2,6-Dimethylazobenzenes					Azobenzenes			
Carbon	C1	C2	C3	C4	CMe	C1	C2	C3	C4
Scale	σ_R^o	σ_R^o	σ_R^o	σ_R^o	σ_R^o	σ_R^+	σ_R^{BA}	σ_R^o	σ_R^{BA}
ρ_I	-1.4	2.0	0.6	2.1	0.9	-0.6	0.6	0.2	1.7
ρ_R	-1.1	2.2	0.6	2.5	0.9	-0.3	0.8	0.3	1.9
λ	0.8	1.1	1.0	1.2	1.0	0.5	1.3	1.5	1.1
f	0.10	0.10	0.11	0.06	0.11	0.32	0.08	0.19	0.10
ρ^{meta}	-1.61	1.92	0.52	1.90	0.85	-0.72	0.59	0.28	1.57
f	0.08	0.06	0.11	0.07	0.06	0.18	0.13	0.32	0.07

Table 25. Changes in Chemical Shift Due to the Resonance Effect of Substituents in *para*-Substituted 2,6-Dimethylazobenzenes and Azobenzenes



Substituent	2,6-Dimethylazobenzenes				Azobenzenes			
X	C1	C2	C3	C4	C1	C2	C3	C4
OMe	0.54	-0.82	-0.23	-1.02	0.26	-0.44	-0.12	-1.00
Me	0.13	-0.14	-0.02	-0.20	0.09	-0.12	-0.04	-0.27
F	0.51	-0.79	-0.19	-0.79	0.16	-0.34	-0.14	-0.74
Cl	0.43	-0.53	-0.14	-0.48	0.13	-0.19	-0.07	-0.43
Br	0.21	-0.41	-0.10	-0.37	0.11	-0.16	-0.07	-0.36
CF_3	0.09	0.04	0.06	0.17	0.05	0.06	0.00	0.16
CO_2Me	-0.13	0.33	0.09	0.37	0.03	0.12	0.01	0.27
Ac	-0.16	0.38	0.12	0.47	-0.14	0.11	0.00	0.34
CN	-0.01	0.22	0.04	0.32	0.07	0.08	0.01	0.24
NO_2	0.11	0.40	0.10	0.48	0.19	0.13	0.01	0.33

discussion we will consider these changes in more detail, concentrating on those at C2 and C4, since these are the ones that clearly, and not unexpectedly, show the greatest sensitivity to resonance effects.

Firstly, the data in Table 25 consists of changes in chemical shift, and as such for each substituent represent the product of its intrinsic resonance effect (σ_R) and a substituent independent measure of the efficiency with which it is relayed to the ring carbon in question (ρ_R). In comparing the results for the 2,6-dimethylazobenzene and azobenzene series, the differences between the two series therefore may arise from either changes in σ_R, changes in ρ_R, or both. For +R groups changes in ρ_R appear to be involved. This can be demonstrated by plotting the resonance components of the shifts for the two series against one another. If σ_R is independent of the series, then the points should lie on a straight line with a slope equal to the ratio of the two ρ_R values. If not then a curve should result. A graph for the C4 carbons is shown in Fig. 8.

The slope of the line through the +R substituents is close to unity, indicating that for this carbon, ρ_R and σ_R are both unaffected by the introduction of the two methyl groups. For -R substituents however the situation is a little different, with all the substituents (except CF_3) lying off the line passing through the +R ones. It is not possible from this data to establish if this behaviour is due to changes in σ_R or ρ_R. The introduction of the two methyl groups, being +I +R in character, into positions where they can interact directly with *para* -R substituents in the other

Fig 8 Resonance Component of the SCS Values at C4, Azobenzene v. 2,6-Dimethylazobenzene

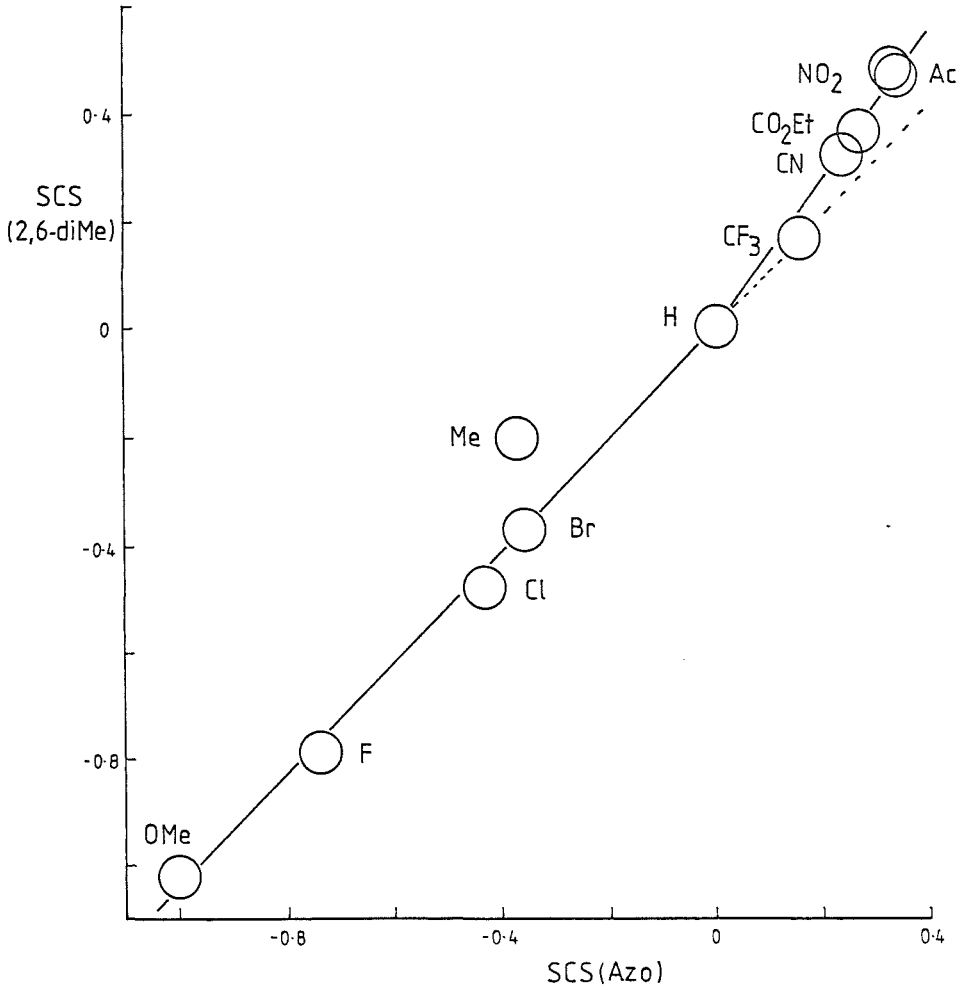
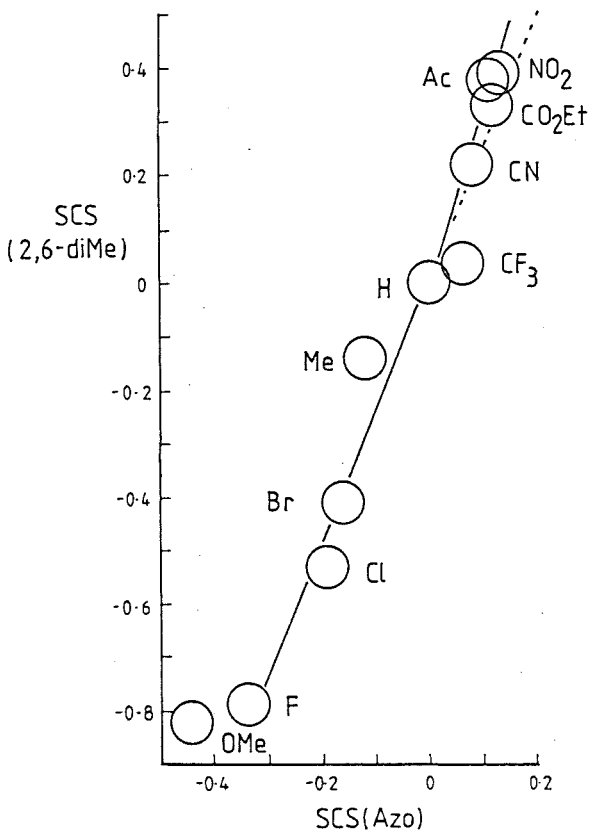


Fig 9 Resonance Component of the SCS Values at C2, Azobenzene v. 2,6-Dimethylazobenzene



ring may offer an explanation for the enhanced resonance contributions observed for -R substituents. Such an interaction could result in either an enhanced efficiency of transmission through the azo linkage (ρ_R), or an enhanced σ_R value for the group.

If a change in σ_R is involved then we might expect this to affect C2 more than C4, while a change in ρ_R should have similar effects on both. A plot for C2, analogous to that for C4 is given in Fig. 9. In this a reasonable line, although not as good as that for C4, is obtained for +R substituents. However, here the presence of the two methyl groups has a much greater effect on the slope, with ρ_R being about twice that for the same carbon in the azo series. For -R substituents we again see an enhancement in the C2 shifts in comparison to the +R ones, but in this case their deviations from the line are much smaller, suggesting that if the differences in behaviour between the two were due to variations in σ_R, then for C2 these are rather small.

In summarizing the situation, therefore, one can say that for *para* +R substituents, introduction of the two methyl groups leads to an approximate doubling of ρ_R at C2, while leaving ρ_R for C4 essentially unchanged. There appears to be little effect on σ_R for these groups. With -R substituents however, the situation is less clear cut. Similar effects on ρ_R are observed, but there may also be slight variations in σ_R as well. The results do not allow us to conclude with any degree of confidence that ρ_R for +R and -R substituents responds differently to the introduction of the methyl substituents.

4.3 The Effect of the Introduced Methyl Groups on ρ_R/ρ_I

The effect of the introduced methyl groups on ρ_I is readily observable since it can be determined using the data for the *meta* substituted derivatives. The situation with regard to resonance effects is somewhat different in that ρ_R can only be determined if we know σ_R for our substituents in the systems under study, and unlike σ_I this is not reaction independent. Separation of this resonance component into the individual ρ_R and σ_R components is possible in theory, but can only be achieved approximately in practice.

At first sight it appears that we are dealing with two unknown variables since both ρ_R and σ_R are unknown. In fact this is not entirely true, since we are dealing with a number of different substituents, and the ratio of their σ_R values can serve as a useful indicator of their position on the σ_R spectrum. This means that the ratios of the resonance components of the SCS values can provide an indication of the σ_R scale applicable. The problem in practice is that we do not know the exact form of the relationship between σ_R and electron demand. We do however know a few fixed points, those corresponding to σ_R^{o}, σ_R^{BA}, σ_R^{+} for +R substituents, and σ_R^{o}, σ_R^{-} for -R ones. Therefore in practice we can compare the observed ratios of the σ_R values to those of the known σ_R scales in order to find one that closely models our observed ratios. Once this is done the ρ_R value for the system can be estimated.

Such an approach has been applied to the resonance components of the SCS values to the C2 and C4 shifts in the 2,6-dimethylazobenzenes and azobenzenes. It has been limited

to the five +R groups (OMe,Me,F,Cl,Br), since our results suggested that these groups had the same σ_R values in both series. The relevant ratios (with the value for p-OMe being taken as unity) are given below, together with the corresponding values for the σ_R^o, σ_R^{BA}, and σ_R^+ scales of Ehrenson, Brownlee and Taft.[8]

	OMe	Me	F	Cl	Br
σ_R^o	1.00	0.24	0.76	0.51	0.42
σ_R^{BA}	1.00	0.18	0.74	0.38	0.31
σ_R^+	1.00	0.25	0.56	0.35	0.29
C2(azo)	1.00	0.27	0.77	0.43	0.36
C4(azo)	1.00	0.27	0.74	0.43	0.36
C2(2,6-diMe)	1.00	0.17	0.96	0.65	0.50
C4(2,6-diMe)	1.00	0.20	0.77	0.47	0.36

For three of the four series the results show that a σ_R scale somewhere in the range between σ_R^o and σ_R^{BA} is appropriate. For C2 in the 2,6-dimethyl series the value for the methoxy group would appear to be anomalously low (it was however, reproducible). (Results based on the fluoro derivative here would be much more in line.) Correlations of the data using the σ_R^o and σ_R^{BA} scales yield the following ρ_R values. (The values for ρ_I are included for comparison purposes):

	$\rho_R(\sigma_R^o)$	$\rho_R(\sigma_R^{BA})$	$\rho_I(=\rho^{meta})$
C2(azo)	1.0	0.7	0.59
C4(azo)	2.2	1.6	1.57
C2(2,6-diMe)	2.0	1.4	1.92
C4(2,6-diMe)	2.3	1.7	1.90

If one assumes that the closer the value of ρ_R is to ρ_I the more likely the σ_R parameter is to be correct, then these results suggest that for all but C2 of the 2,6-dimethyl series, the appropriate σ_R parameter lies closer to σ_R^{BA} than σ_R^o. A more reliable guide, however, is provided by considering the intercepts of the correlations, and in particular those for correlations where the unsubstituted derivative is not used. These are listed below.

	Intercept	
	ρ_R^o	ρ_R^{BA}
C2(azo)	+0.01	-0.04
C4(azo)	-0.04	-0.09
C2(2,6-diMe)	-0.01	-0.14
C4(2,6-diMe)	+0.08	-0.07

A negative intercept implies that the σ_R scale chosen is on the high side, a positive one, on the low. This approach leads to a rather different conclusion. It suggests that for C2 in both series the σ_R^o scale is the most appropriate one, while for C4 an intermediate one between σ_R^o and σ_R^{BA} is required. If this is the case then it means that ρ_R/ρ_I is around unity

in the 2,6-dimethylazobenzene series for both C2 and C4 carbons, but significantly greater than unity (25-50%) for the corresponding carbons in the azobenzene series.

Although the ρ_R values obtained are only approximate, their similarity to the ρ_I values demonstrates that the two may not be entirely independent. If this is so, then there are at least two possible explanations for this phenomenon. One is that similar transmission mechanisms are involved, i.e. the π system in both cases. Since Reynolds claims that the π-inductive effect is the main mechanism for the relay of field effects in conjugated π-systems, then this explanation would not seem unreasonable. However this interpretation can not explain why both ρ_I and ρ_R for C2 in the 2,6-dimethyl-azobenzenes are about twice that in the azobenzenes. It would in fact predict that both would be <u>less</u> if the methyl groups forced the xylyl group out of the plane of the rest of the molecule.

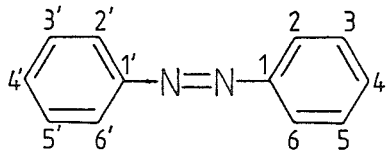
The second possible explanation is that regardless of the effect of any loss of coplanarity on ρ_I and ρ_R, for C2 the main reason for their substantial increase in magnitude is related to the presence of the methyl group on this carbon. The methyl group shifts the resonance position for C2 downfield by about 8 ppm, indicating a considerable change in the environment of the carbon. This could easily have a big influence on the intrinsic sensitivity of the C2 carbon to substituent effects and could influence ρ_I and ρ_R approximately equally. But it should be noted that a similar effect is not observed for C_β in the β,β-dimethylstyrenes.[107] Here the presence of the two methyl groups has little effect on ρ_I and ρ_R.

On the whole it would appear that there are so many factors that are potentially capable of affecting ρ_I and ρ_R for the C2 carbon that there seems little to be gained by further speculation at this time.

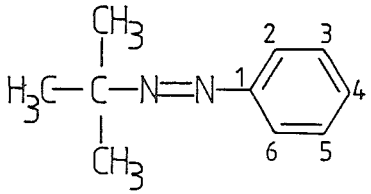
In conclusion, it is clear that the effect that we thought we would see in going from the azobenzene to the 2,6-dimethylazobenzene systems, a decrease in the ρ_R/ρ_I ratio at C2 and C4, has occurred, but it is rather small and has been more than offset by increases in individual ρ_R and ρ_I values. This means that the data do not provide us with unambiguous evidence either for or against any loss of planarity of the system resulting from the presence of the two methyl groups. For the case of C4, the ring carbon *para* to the phenylazo group, the presence of the two methyl groups has little overall influence on the SCS values. Since, on the basis of the results obtained in Part I, they apparently have a substantial one on reactions of functional groups in this position, then this implies that the geometries in the two systems are different. If this is so then one is forced to the conclusion that, in the systems studied in Part I, the phenylazo or t-butylazo group undergoes a change in geometry in going from the ground to transition state, while no such change takes place during the absorption and emission of energy during the nuclear magnetic resonance process.

Appendix ^{13}C n.m.r. Data for the Azobenzenes, t-Butylazobenzenes and the Azoxybenzenes Studied

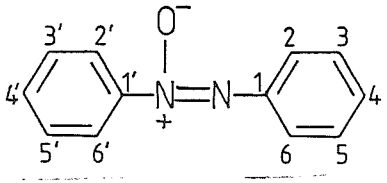
The ^{13}C n.m.r. chemical shifts of the carbon atoms of the compounds studied are listed in the following pages. In all cases the chemical shift (δ) is quoted in p.p.m. downfield from tetramethylsilane. Missing figures indicate that peaks were not observed.



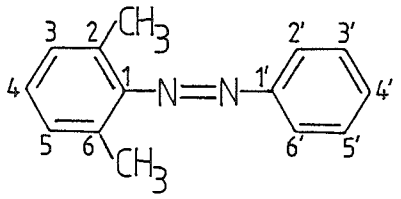
Substituent	Carbon 1'	2'	3'	4'	5'	6'	1	2	3	4	5	6	X				
H	152.72	122.89	129.09	130.98	129.09	122.89	152.72	122.89	129.09	130.98	129.09	122.89					
3-CO_2Me	152.48	123.03	129.14	131.37	129.14	123.03	152.57	124.06	122.91	131.63	129.14	126.89	166.49	52.29			
4-CO_2Et	152.58	122.60	129.16	131.64	129.16	122.60	155.11	123.16	130.56	132.22	130.56	123.16	166.00	61.22	14.34		
4-CH_2-CO_2Et	152.71	122.84	129.10	130.98	129.10	122.84	151.76	123.09	130.04	137.24	130.04	123.09	42.33	171.07	61.62	14.17	
2,6-diMe	152.83	122.51	129.10	130.96	129.10	122.51	151.52	130.61	129.10	128.09	129.10	130.61	18.76				
2,6-diMe-4-CO_2Et	152.67	122.68	129.19	131.60	129.19	122.68	154.98	130.11	130.27		130.27	130.11	18.41	166.34	60.94	14.36	
2,6,2',6'-tetraMe	151.41	131.25	129.39	128.41	129.39	131.25	151.41	131.25	129.39	128.41	129.39	131.25	19.77				
2,6,2',6'-tetraMe-4-CO_2Et	150.77	132.03	129.62	129.25	129.62	132.03	155.06	129.37	130.50	128.94	130.50	129.37	19.33	20.00	166.31	60.98	14.39
4-CMe_2OH	152.76	122.76	128.96	130.78	128.96	122.76	152.15	122.66	125.19	151.28	125.19	122.66	72.42	31.60			
2,6-diMe-4-CMe_2OH		122.50	129.09	130.89	129.07	122.50		(130.68)	125.09	149.06	125.09	(130.68)	19.19	72.41	31.74		
2,6,2',6'-tetraMe-4-CMe_2OH	149.35	131.57	129.38	128.31	129.38	131.57	151.60	131.17	125.56	149.89	125.56	131.17	19.76	20.21	72.41	31.74	
4'-OMe-4-CMe_2OH	147.10	124.69	114.20	162.00	114.20	124.69		122.44	125.15	151.45	125.15	122.44	55.55	72.54	31.75		
4'-Me-4-CMe_2OH	151.81	122.81	129.69	141.35	129.69	122.81	150.83	122.60	125.15	151.52	125.15	122.60	21.44	72.57	31.71		
4'-F-4-CMe_2OH		125.03 124.58	116.56 115.42		116.56 115.42	125.03 124.58	152.20	122.71	125.25		125.25	122.71	72.58	31.74			
4'-Br-4-CMe_2OH	151.40	124.31	132.31		132.31	124.31	151.26	122.84	125.28	152.53	125.28	122.84	72.60	31.74			
3'-Br-4-CMe_2OH	153.60	124.64	123.13	133.48	130.40	122.89	152.23	122.98	125.28	152.77	125.28	122.98	72.59	31.77			



	carbon											
Substituent	1	2	3	4	5	6	C	Me_3	X			
3-CO_2Me	152.46	123.26	131.17	130.79	128.98	126.14	68.14	26.95	166.62	52.22		
3-CO_2H	150.89	122.39	128.60	129.74	127.54	125.33	66.65	25.34	170.26			
4-CO_2Et	155.03	121.72	130.46	131.48	130.46	121.72	68.45	26.91	166.09	61.12	14.32	
4-CO_2H	155.75	121.87	131.25	130.21	131.25	121.87	68.69	26.90	171.91			
4-CMe_2OH	150.98	121.73	124.95	151.12	124.95	121.73	67.53	26.96	72.46	31.75		
2,6-diMe-4-CO_2Et		127.97	130.06	128.31	130.06	127.97	69.87	26.94		60.88	14.35	17.43
2,6-diMe-4-CO_2H	156.62	128.10	130.75	130.64	130.75	128.10	70.00	26.92	172.04	17.41		
2,6-diMe-4-CMe_2OH	150.62	128.12	124.55	147.50	124.55	128.12	69.18	27.04	72.32	17.94	31.77	



	carbon															
Substituent	1′	2′	3′	4′	5′	6′	1	2	3	4	5	6	X			
H	148.2	122.2	128.5	131.3	128.5	122.2	144.0	125.4	128.5	129.4	128.5	125.4				
4-Br		122.21	128.70	131.68	128.70	122.21	142.72	127.09	131.77	123.09	131.77	127.09				
4′-Br		123.82	131.82	126.07	131.82	123.82	143.69	125.58	128.65	129.82	128.65	125.58				
4-CN	147.80	122.35	128.94	132.73	128.94	122.35	146.86	125.67	132.56	112.00	132.56	125.67	118.40			
4′-CN		123.18	132.85	115.22	132.85	123.18	143.46	125.87	128.84	130.60	128.84	125.87	117.57			
3-CO_2Et		122.22	128.80	131.83	128.80	122.22	144.04	126.90	131.19	130.22	128.71	129.09	165.86	61.18	14.53	
3′-CO_2Et	148.44	123.50	131.6	132.41	128.94	126.41	144.83	125.73	128.75	129.97	128.75	125.73	165.27	61.57	14.30	
4-CO_2Et		122.40	128.84	131.98	128.84	122.40	147.21	125.09	130.04	130.56	130.04	125.09	165.71	61.09	14.30	
4′-CO_2Et	150.98	122.35	130.25	133.15	130.25	122.35	143.79	125.81	128.75	130.16	128.75	125.81	165.28	61.47	14.20	
4-CO_2Me		122.42	128.89	132.02	128.89	122.42	147.32	125.10	130.12		130.12	125.10	166.25	52.20		
2,6-diMe-4-CO_2Et		122.54	129.03	132.40	129.03	122.54	146.81	130.25	129.41	128.79	129.41	130.25	166.48	60.87	14.38	17.51
2,6-diMe-4-CMe_2OH		122.55	128.92	132.07	128.92	122.55	141.35	129.73	124.26	147.69	124.26	129.73	72.36	31.74	17.87	
4-COMe		122.84	128.89	132.10	128.89	122.84		125.29	128.89	136.89	128.89	125.29	191.15	26.50		
4′COMe		122.66	128.94	139.16	128.94	122.66	143.79	125.80	128.80	130.21	128.80	125.80	195.45	26.80		
4-CMe_2OH		122.32	128.69	131.51	128.69	122.32		124.91	124.80		124.80	124.91	72.53	31.63		
4′CMe_2OH	153.14	122.18	124.97	172.70	124.97	122.18	144.00	125.54	128.67	129.59	128.67	125.54	72.37	31.70		



Substituent	Carbon 1'	2'	3'	4'	5'	6'	1	2	3	4	Me_2	X		
H	152.83	122.51	129.10	130.96	129.10	122.51	151.52	130.61	129.10	128.09	18.76			
3'-OMe	154.02	105.81	160.35	117.44	129.79	116.60	151.41	130.57	129.10	128.13	18.75	55.42		
4'OMe	147.21	124.31	114.16	162.10	114.16	124.31	151.66	130.27	129.00	127.54	18.65	55.56		
3'-Me	152.93	122.90	139.01	131.75	128.91	119.87	151.66	130.42	129.06	127.96	18.70	21.35		
4'-Me	151.00	122.53	129.72	141.52	129.72	122.53	151.68	130.43	129.07	127.85	18.68	21.43		
4'-F		124.71 124.27	116.59 116.47	170.80 158.20	116.59 116.47	124.71 124.27	151.23	130.78	129.17	128.25	18.85			
3'-Cl	153.66	121.88	135.18	130.64	130.12	121.53	150.85	131.25	129.25	128.72	19.04			
4'-Cl	151.03	123.72	129.33	136.91	129.33	123.72	151.21	130.96	129.20	128.48	18.94			
3'-Br	153.75	124.46	123.14	133.54	130.42	122.37	150.84	131.25	129.25	128.75	19.04			
4'-Br	151.53	123.97	132.32	125.39	132.32	123.97	151.02	131.04	129.23	128.56	18.99			
3'-Ac	152.91	122.93	138.22	130.25	129.42	126.10	150.96	131.17	129.28	128.73	19.04	194.77	26.74	
4'-Ac	155.17	122.50	129.37	138.42	129.37	122.50	150.91	131.53	129.37	120.09	19.18	194.92	26.76	
3'-CO_2Me	152.84	124.11		131.67	131.39	126.07	151.02	131.20	129.24	128.66	19.04	166.51	52.31	
4'CO_2Et	155.26	122.23	130.60	132.21	130.60	122.23	150.97	131.44	129.33	128.95	19.14	166.01	61.23	14.34
3'-CF_3	152.87	119.51		127.23	129.72	125.60	150.82	131.49	129.38	129.04	19.13			
4'-CF_3	154.60	122.70	126.34		126.34	122.70	150.89	131.51	129.40	129.11	19.14			
3'-CN	152.76	125.72		133.68	130.10	127.00	150.37	131.87	129.45	129.45	19.33	113.46		
4'CN	154.67	122.98	133.24	118.44	133.42	122.98	150.48	132.06	129.48	129.62	19.37	113.94		
3'-NO_2	153.26	116.94	129.33	124.85	129.98	128.46	150.29	132.07	129.50	129.50	19.42			
4'NO_2	155.85	123.00	124.75		124.75	123.00	150.49	132.37	129.57	129.92	19.51			

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ACKNOWLEDGEMENTS

I am indebted to the Department of Chemistry of the University of Canterbury for the award of a Teaching Fellowship during the tenure of which this work was carried out.

I would also like to express my thanks to my supervisor, Dr D.A.R. Happer, and to Professor M.P. Hartshorn for his supervision during Dr Happer's study leave. I also thank Mrs K. Buckner for the typing of this thesis, Mr Michael Hay for proof-reading the manuscript, and the staff and technicians of the Chemistry Department for their assistance.